

103

MARINE BIOTECHNOLOGY

Y 4.M 53:103-26

HEARING

Marine Biotechnology, Serial No. 10... OF THE

SUBCOMMITTEE ON OCEANOGRAPHY, GULF OF
MEXICO, AND THE OUTER CONTINENTAL SHELF

OF THE

COMMITTEE ON
MERCHANT MARINE AND FISHERIES
HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRD CONGRESS

FIRST SESSION

ON

THE IMPORTANCE OF MARINE BIOTECHNOLOGY
IN SPAWNING NEW INTERESTS IN AQUACUL-
TURE, DISCOVERING NEW INDUSTRIAL AND
BIOCHEMICAL PRODUCTS, AND DEVELOPING
NEW TECHNIQUES FOR MARINE RESEARCH

APRIL 29, 1993

Serial No. 103-26

Printed for the use of the Committee on Merchant Marine and Fisheries



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MARINE BIOTECHNOLOGY

THURSDAY, APRIL 29, 1993

HOUSE OF REPRESENTATIVES, SUBCOMMITTEE ON OCEANOGRAPHY, GULF OF MEXICO, AND THE OUTER CONTINENTAL SHELF, COMMITTEE ON MERCHANT MARINE AND FISHERIES,

Washington, DC.

The Subcommittee met, pursuant to call, at 10:02 a.m., in room 1334, Longworth House Office Building, Independence Avenue, Hon. Solomon P. Ortiz [chairman of the Subcommittee] presiding. Present: Representatives Ortiz, Studds, Weldon, and Green. Staff present:

STATEMENT OF HON. SOLOMON P. ORTIZ, A U.S. REPRESENTATIVE FROM TEXAS, AND CHAIRMAN, SUBCOMMITTEE ON OCEANOGRAPHY, GULF OF MEXICO, AND THE OUTER CONTINENTAL SHELF

Mr. ORTIZ. Good morning. I would like to welcome all of you here today on behalf of the Subcommittee on Oceanography, Gulf of Mexico, and the Outer Continental Shelf.

Today the Subcommittee meets to examine the promise and future offered through advances in the field of marine biotechnology. The Subcommittee recognizes the importance of marine biotechnology, both scientifically and economically, and the potential of this field of study to boost U.S. competitiveness.

Many promising advances have already been made, spawning new industries in aquaculture, discovering new industrial and biochemical products, and developing new techniques for marine research.

However, this progress is minimal compared with advances made in the non-marine biotechnology fields. The primary reason for this discrepancy is the relative lack of Federal investment in marine biotechnology.

The Administration's fiscal year 1994 budget request includes five Presidential initiatives identified by the Federal Coordinating Council for Science, Engineering, and Technology as critical to the Nation's future technological strength, economic growth, and the health and quality of life.

Included in these initiatives are biotechnology, climate and global change, and high-performance computing and communication. In fact, biotechnology was the largest of these initiatives in the fiscal year 1994 funding request at over \$4 billion dollars, however the vast majority of this request is for non-marine research.

The total Federal investment in marine biotechnology is only about \$50 million dollars, or 1.25 percent of the total. Of that, approximately \$5 million dollars is provided for university-based research through NOAA's National Sea Grant College Program.

It is clear that the U.S. has the potential to be a world leader in the marine biotechnology field. But the race has already begun. The Japanese government invests \$180 million dollars annually in marine biotechnology, in comparison to \$50 million dollars by the United States.

It is time for the United States to expand biotechnology efforts into the ocean and make a concerted investment in our future. Towards this end, the Committee, led by Chairman Studds, is considering legislation to create a marine biotechnology research program within the Sea Grant program. The bill would establish Sea Grant as a national leader for marine biotechnology research, taking advantage of the existing research, education and technology transfer infrastructure.

I look forward to hearing your testimony today concerning this exciting field, and I am particularly interested in hearing the panel's comments on the proposed legislation.

I know that our distinguished Chairman, Mr. Studds, will have to go testify before another committee, and at this time, Mr. Chairman, if you have a statement to make?

STATEMENT OF HON. GERRY E. STUDDS, A U.S. REPRESENTATIVE FROM MASSACHUSETTS, AND CHAIRMAN, COMMITTEE ON MERCHANT MARINE AND FISHERIES

Mr. STUDDS. Thank you very much, Mr. Chairman. I won't keep you very long. I apologize, I do have to go defend the honor, in fact the existence, of this committee before another committee.

I really want to thank you for holding this hearing. As you know, I think marine biotechnology is an area of great importance and promise for U.S. science and technology, not only in my own part of Massachusetts where it is preeminently important, but for the country as a whole.

If we are going to remain competitive in the global marketplace, we need to play to our strengths and back a winner, and marine biotech is a winner.

To help support this industry, I yesterday introduced the Marine Biotechnology Investment Act, a bill that creates a grant program through Sea Grants for research, development and technology transfer and education in marine biotechnology.

Although Federal support, as you pointed out for biotech in general, has been good, marine biotech has not sufficiently benefited, and that is going to change with your help.

I would like to welcome the distinguished panel of witnesses, in particularly Dr. John Burris, Director of the Marine Biological Laboratory in Woods Hole. That venerable institution as I think you know, Mr. Chairman, is at the forefront of marine biotechnology research.

I would also like to welcome Dr. Joseph Chang from Boston, whose company is involved in precisely the kind of cutting-edge re-

search that illustrates both the promise and the challenge of marine biotechnology.

I profoundly apologize to all of the witnesses for my inability to be in three places at one time. Perhaps if you were physics folk you could work that problem out; I haven't solved it. My heart, however, and soul and legislation will be here when I leave. I wish you well, and I assume you will proceed to markup by the end of the day. Thank you, Mr. Chairman.

Mr. ORTIZ. Thank you. I would like to also welcome the ranking member of the Subcommittee, Mr. Weldon, and he will attempt to make any statement that he would like to make this morning.

STATEMENT OF HON. CURT WELDON, A U.S. REPRESENTATIVE FROM PENNSYLVANIA

Mr. WELDON. Thank you, Mr. Chairman, and I too appreciate you holding this hearing and will look forward to the testimony today.

I apologize in advance for having to run out of this hearing. I also have other hearings going on that I am involved in on other committees.

I am loyally interested in this issue. Marine biotechnology is a crucial component to improving our resources through processes such as bioremediation. We are able to design effective programs to improve the marine environment; however, in order to accomplish this, it is imperative that we utilize both our commercial and scientific potential.

I think it is very important that marine biotechnology serves as a means for improving the marine environment. There are a number of commercial and research institutions that are researching marine biotechnology. These efforts have only proven what many have long suspected; that marine biotechnology is an effective and important approach to marine research.

It is now time, however, to ensure that these efforts are encouraged. Legislation such as the Marine Biotechnology Investment Act of 1993 are a good start. However, creating effective programs to stimulate further research is crucial.

I hope that today's discussion will focus on marine biotechnology research efforts currently underway in both the public and private sectors as well as the future of this area. I also hope to explore what long-term goals and direction the field of marine biotechnology hopes to take.

As I am sure many who are present today will recall, this Subcommittee recently held a hearing on the National Undersea Research Program. One of the points that was continuously raised was the need to develop an effective and comprehensive long-range plan for undersea research.

Perhaps a similar long-term comprehensive plan is also necessary for marine biotechnology.

Finally while I strongly support marine biotechnology, I do share similar concerns of other members on this committee. While the Sea Grant Program continues to be an effective research vehicle, it has been seriously underfunded.

If legislation, such as the Marine Biotechnology Investment Act were enacted, I feel it is imperative that adequate funding exists

for both ongoing and future sea grant programs as well as marine biotechnology research.

I want to thank you for again holding this hearing and ask unanimous consent to submit both my written statement into the record and the statement of the Honorable ranking Republican on the full committee, Jack Fields.

Mr. ORTIZ. Hearing no objections, so ordered.

[The prepared statement of Mr. Fields follows:]

STATEMENT OF HON. JACK FIELDS, A U.S. REPRESENTATIVE FROM TEXAS, AND
RANKING MINORITY MEMBER, COMMITTEE ON MERCHANT MARINE AND FISHERIES

Mr. Chairman, thank you for convening this hearing today on the fascinating topic of marine biotechnology.

I have cosponsored Chairman Studds' Marine Biotechnology Investment Act, not only because biotechnology holds so much promise, but also because I know that universities in Texas have been in the vanguard of research into this area. In fact, several proposals submitted this year by Texas A&M University to the National Sea Grant Program have concentrated on marine biotechnology, especially as it relates to improved opportunities for aquaculture in the Gulf of Mexico. A marine biotechnology initiative was begun by Sea Grant under President Bush and it continues today, and I am pleased to see it legislatively expanded.

However, I do have two concerns about the Chairman's proposed legislation. The first is a concern that the marine biotechnology program created by this bill may grow at the expense of the core National Sea Grant College Program. I would hate to see the valuable work already conducted under the Sea Grant auspices short-changed while a new program is created. It is my hope that Chairman Studds will make clear to the Appropriations Committee that new funds are needed for this initiative. In addition, I find the establishment of a separate review panel only for marine biotechnology grant proposals troubling. If the current Sea Grant review process is insufficient, then we should beef it up so that all Sea Grant scientific grants receive the same rigorous peer review as outlined in this bill.

Having said that, I look forward to testimony from our distinguished witnesses, especially Dr. Samuel Wilson from the Sealy Center for Molecular Science at the University of Texas.

Thank you, Mr. Chairman.

Mr. ORTIZ. Does the distinguished gentleman from Texas have a statement?

Mr. GREEN. Thank you, Mr. Chairman. I have no prepared statement, but I would just like to welcome a fellow Texan from the University of Texas to the panel. And I also share the concern of all the members for the expansion in additional research in marine biotechnology. The district I represent is in the Houston area. Obviously, we have a great deal of medical facilities there, just like we do in Galveston, where one of our panel members is from. So I look forward to the testimony, but also considering the bill.

Mr. ORTIZ. Thank you. We are very happy to have a very distinguished panel this morning, which consists of, first is Dr. John Burris, Director of the Maine Biological Laboratory in Woods Hole, Massachusetts. Dr. Burris is also the former Executive Director of the Commission on Life Sciences for the National Resource Council.

We also have Dr. Rita Colwell, who is the President of the American Biological Institute of the University of Maryland System. Dr. Colwell is also the former Director of the Maryland Sea Grant Program.

Next is Dr. Samuel Wilson, the Director of the Sealy Center for Molecular Science and Professor of Human Biological Chemistry and Genetics for the University of Texas Medical Branch.

Dr. Ned Ostenso is the Assistant Administrator for Oceanic and Atmospheric Research of the National Oceanic and Atmospheric Research.

Dr. Joseph Chang, who was introduced also by Mr. Studds, is the President of Osteoarthritis Sciences, Incorporated.

Last but not least is Dr. Lawrence Koskan, President of Donlar Corporation, which sells special proteins for industrial and consumer uses.

Thank you for being with us and we will begin with Dr. John Burris. Doctor.

STATEMENT OF DR. JOHN BURRIS, DIRECTOR AND CHIEF EXECUTIVE OFFICER, MARINE BIOLOGICAL LABORATORY, WOODS HOLE, MASSACHUSETTS

Dr. BURRIS. Thank you, Mr. Chairman and members of the Subcommittee for the opportunity to testify today on the importance of marine biotechnology and the need for a stronger Federal role in this area.

My name is John Burris, and I am Director and Chief Executive Officer of the Marine Biological Laboratory in Woods Hole, Massachusetts, the oldest marine biological lab in the United States and one of the leading institutions in the field of marine biotechnology in the world today.

Marine biotechnology represents an extraordinary opportunity to achieve a wide range of objectives, such as promotion of economic growth and stimulation of new business opportunities, development of new environmental and biomedical technologies, and the improvement of America's global economic competitiveness in an emerging growth industry in which the U.S. currently leads.

Marine biotechnology offers a broad range of applications that will revolutionize our ability to better use marine resources.

I would like to take the opportunity now to highlight a few of these promising applications.

First, considerable effort has been and is being directed to searching for pharmaceuticals and diagnostics from the marine environment with encouraging results that include an analgesic and antiinflammatory agent from a marine sponge, an anticancer drug from a sea squirt, and a new class of antibiotics that are active against bacteria and the causative agent of malaria.

Diagnostics include an extract from the horseshoe crab used to test for endotoxin.

Second, a wide variety of biomaterials come from or are being sought from the sea. These include biopolymers extracted from algae that are used to culture bacteria and improve the texture of ice cream and paints.

Another polymer from the foot of the common blue mussel is an adhesive protein that may be used to repair knee ligaments or in dental cavities and skin grafts.

The high-temperature stable enzymes isolated from bacteria found in deep sea vents have been commercialized for use in laboratories and may now be used in other high-temperature applications such as laundry detergents.

Third, marine biotechnology has important applications in aquaculture and seafood safety. With a 1989 trade deficit of \$4.9 billion dollars in fisheries products in the U.S., it is clear that a market exists for seafood products.

Enhancement of marine aquaculture using biotechnology is one way to help meet some of that demand. For example, the use of growth hormone with freshwater fish has led to remarkable increases in their growth rates. The breeding of a triploid strain of oysters now allows year-round oyster production rather than just seasonal production.

As Americans continue to eat progressively more seafood each year, the safety of that seafood will be of paramount concern. Marine biotechnology offers sophisticated tests that will enable assays for ciguatoxin, a poison in fish, and *Vibrio cholerae*, the causative agent of cholera in oysters.

Fourth, bioremediation, the use of organisms to clean up the environment is another important application of marine biotechnology. By systematic screening of naturally occurring microorganisms or the enhancement of desired traits through genetic manipulation, scientists and engineers are working to develop super bugs that attack and break down oil and other bacteria that are able to remove toxic metals and metabolize industrial wastes.

Fifth, products of biotechnology are important scientific tools that enable us to learn more about marine life and the ocean environment.

Genetic probes that allow us to track specific populations of organisms, such as salmon stocks, can tell us a great deal about the movement and origin of the organisms and the waters in which they are found.

The techniques used in biotechnology will also help us learn more about the cycling and consumption of elements and compounds such as carbon dioxide, nitrogen and phosphorus.

Marine biotechnology offers great opportunities, but it is woefully underfunded.

As the Chairman stated earlier, biotechnology is by far the largest interagency initiative in the feeset process, at more than \$4 billion dollars in the President's budget request for fiscal 1994.

However, marine biotechnology is a neglected stepchild in this process. Only about one percent of this initiative is for marine biotech research. Total funding for marine biotech has been virtually flat since 1988.

The lack of attention in the U.S. stands in sharp contrast to the high level of interest being shown in other countries. Japan in particular has embarked on a forward-looking investment strategy in which industry and government have agreed to provide nearly \$200 million dollars for marine biotech in a decade-long program under the auspices of the Ministry of International Trade and Industry.

While the U.S. is currently the world leader in marine biotech, we will not retain this lead for long if we fail to respond to the competitive challenge we face.

It is essential to promote mechanisms for technology transfer together with partnerships between industry, academia, and the government to enable U.S. firms to bring products to the marketplace.

I believe that the recently introduced Marine Biotechnology Investment Act fulfills this objective and more. It establishes a broad-based program within Sea Grant, together with a process to ensure that the proposals are funded on the basis of scientific merit.

It fosters the public/private partnerships that are needed to produce the products that will create jobs and economic growth. And it supports the training and education that will be needed to ensure that we have the human resources that are required.

Mr. Chairman, I want to commend you for holding this hearing and for playing a leadership role in bringing much needed attention to the enormous potential of marine biotechnology. And I want to express my appreciation to Chairman Studds for his leadership in introducing important legislation. I urge the quick passage of the Marine Biotechnology Act.

I would add one further note. One never knows in funding what the results will be or one cannot predict precisely what they will be. This is clearly exemplified in a recent article published in "Science Magazine" by a scientist at the Marine Biological Laboratory, Mitchell Sogin.

Dr. Sogin has shown the interrelatedness of fungi and animals. In so doing through very basic scientific techniques, he has opened up a wide variety of potential biomedical applications and information. Given our knowledge that fungi are related to animals, may have important implications for how we treat fungal diseases pharmaceutically.

Dr. Sogin has also showed that Pneumocystis, one of the main causes of death in AIDS patients is more closely related to fungi than to protozoa. Before his techniques were applied it was uncertain what type of organism this was. This again has led to potential applications in the treatment of the disease.

So, again I repeat, one should consider seriously passage of the Marine Biotechnology Investment Act. I am firmly in favor of it and would be happy to answer any questions. Thank you, Mr. Chairman.

[The prepared statement of Dr. Burris can be found at the end of the hearing.]

Mr. ORTIZ. Thank you, Dr. Burris. Dr. Colwell, you may proceed.

STATEMENT OF DR. RITA R. COLWELL, PRESIDENT, MARYLAND BIOTECHNOLOGY INSTITUTE, UNIVERSITY OF MARYLAND

Dr. COLWELL. Thank you, Mr. Chairman and members of the Subcommittee. I am Rita Colwell, founder and President of the Maryland Biotechnology Institute of the University of Maryland System. The MBI comprises four centers that conduct research and training in biotechnology, one of which is the Center of Marine Biotechnology, established in Baltimore in 1985. COMB is an emerging center of marine biotechnology that combines traditional marine sciences with molecular biology and molecular genetics.

I wish to emphasize the views just expressed by Dr. Burris on the unquestionable need for funding in the area of marine biotechnology research and development.

I have devoted most of my career to the study of marine microorganisms, and I cannot overemphasize the importance of marine bio-

technology. It is one of the most exciting areas of the new scientific frontier, if only for the sheer raw potential of the great diversity of marine organisms within the world's oceans, which constitute 75 percent of the earth's surface.

Marine biotechnology has made many extraordinary advances, some of which Dr. Burris has described. COMB in Baltimore has contributed advances, including production of the first transgenic fish by taking the growth hormone cloned from the trout and introducing it into carp for a bigger, faster-growing fish. This development is important for Third World nations, which depend on fish as a major source of protein.

The advances in the field are resulting in a wide range of applications. I would say that biotechnology is to society really very similar to the invention of a steam engine, the computer, and the splitting of the atom. And I would emphasize to you that the status of marine biotechnology is analogous to that of the semiconductor industry in the late 1960's: we are on the brink of a scientific revolution with incredible implications for the world's financial markets.

The question we have before us is whether it will be us, in the United States, or our international competitors, that ultimately profit from this promising new technology.

To assess the prospects of marine biotechnology, the MBI, supported by Sea Grant funds, recently established a data base to assess the status of marine biotechnology research and related industries in the U.S., Japan, the Scandinavian countries, and other industrialized countries.

The preliminary findings of my colleagues and I were published earlier this month. I have included a copy with my written testimony, and I ask that it be submitted for the record.

We found that in the United States, marine biotechnology is very much in the formative stage and that advances in the basic biological sciences really drive the development of the field. Despite the field's relatively small size and minuscule funding level, marine biotechnology has been surprisingly productive. In fact, we estimate that one patent has been approved for every \$1.1 million spent at universities and public research centers.

We found that about 80 U.S. companies were dedicated to marine biotechnology or were sponsoring marine biotechnology research and development. Most of that, however, is in the natural products area. The other areas of bioremediation, aquaculture, and new commercial product development are still very much in the developmental stage.

Our data also indicate that significant advances made so far in aquaculture have not been demand-driven, as many people believe, but rather resulted from technological advancements, most notably in genetic selection and in the ability to select for disease-resistant strains.

Overall, we found that U.S. industry has played only a minor role in marine biotechnology for three reasons: First, marine biotechnology and its promises are practically unknown to many firms, which perceive it as too much of a risk when offered the opportunity to enter the field. Second, most of the applications will be generated in the medium- to long-term, and U.S. companies, as you

well know, particularly the smaller start-ups, are underfunded and tend to plan only for short-term, three- to five-year cycles. That excludes many of the research directions that we need in marine biotechnology, which is a relative newcomer.

Third, unresolved issues with respect to field testing and the release of genetically engineered organisms, especially into the marine environment, have produced some uncertainties among companies. These can and should be addressed through research that we propose to do in the next three or four years.

The ocean industry contributes more than \$100 billion annually to the U.S. economy, with about \$25 billion and one million jobs coming from fisheries alone. I believe that this demonstrates that this is an area in which we have tremendous advantages if we invest wisely.

But despite these figures, total Federal funding for marine biotechnology, as Dr. Burris pointed out, was only about \$44 million in fiscal year 1992. Funding for fiscal year 1993 increased by about \$6 million, which is quite trivial. Federal funding for marine biotechnology research is only about one percent of the total Federal biotechnology budget. So it is clear that we do need a greater investment in this area.

I would point out that in funding the Center of Marine Biotechnology in Baltimore in 1985, we received funding from the Office of Naval Research under the University Research Initiatives. But unfortunately, funding in all agencies has remained absolutely flat for the past three years, and there really hasn't been any real growth in that time for marine biotechnology, nor can we expect any during the next three years. This makes this bill critical.

Coordination of Federal, academic and industry efforts is absolutely critical for this field. And unless a concerted national effort designed to yield to marine biotechnology advances and progress is launched by the Federal Government, academia and industry, the U.S. is simply going to lose leadership to countries such as Japan, China, Taiwan, Thailand, Norway, Iceland, and Sweden. The U.S. advances will be limited to occasional chance discoveries of a process or application and very likely end up being patented and licensed for overseas manufacture.

As you have learned from other witnesses today, Japan, through a consortium of academic, government and industrial organizations, has seized upon marine biotechnology, has taken the lead, and is working toward a ten-year objective. In fact, at the Center of Marine Biotechnology in Baltimore, we have hosted dozens of delegations from Japan, scientists who wish to study our Marine Biotechnology Center as a model before setting up their own centers—a bit frustrating, actually. And backing up this intensive national interest by Japan is significant financial investment in what they clearly believe to be a promising technology of the future.

Mr. Chairman, I believe that the bill before this committee is exactly what is required to ensure that the U.S. stays at the forefront of this very promising frontier and does not relinquish yet another important new technology to overseas competitors.

I have long been on record that one of the best things our government has done is to establish the National Sea Grant College Program. It is really a tragedy for this nation that the budget of

Sea Grant, which provides a 20-fold return on Federal investment, has declined in real terms by more than 50 percent since 1979.

Sea Grant has been at the forefront of marine biotechnology funding for more than 2 decades, despite the small amount of money available for marine biotechnology, and has essentially kept it alive.

When I leave here this morning, I will be heading for the Center of Marine Biotechnology in Baltimore to announce at a press conference that one of our researchers has been successful in culturing in the laboratory one of the two disease agents that has devastated oyster populations and almost destroyed the oyster industry in the Chesapeake Bay in Maryland.

The breakthrough comes at the end of one of the worst oyster harvests in Maryland history, caused in large part by increasing levels of this pathogen. Last Sunday, the *Baltimore Sun* ran an editorial about the plight of the oyster, essentially recommending resignation to the vagaries of nature and the ravages of these diseases on Maryland's signature water industry.

But with this new knowledge, which we will be announcing today, provided by marine biotechnology, researchers will now be able to begin to develop gene probes to diagnose the pathogen in infected oysters in the Chesapeake Bay and to genetically engineer drugs that will stop the infection or to produce resistant strains of the oyster.

The finding will have enormous implications for the oyster industry as well as the health of the Chesapeake Bay. This breakthrough was made possible through Sea Grant funding.

I wish to register strong support for the way by which the new funds will be administered. The bill establishes a national review process that will award grants based on merit and ensures that projects will be evaluated competitively, and on a level playing field. This is the best way to ensure that only proposals of the highest quality and promise are funded.

Mr. Chairman, to summarize, marine biotechnology represents one of the greatest frontiers of intellectual and commercial endeavors in the marine sciences. NIH is turning to natural products and to traditional forms of medicine, and centuries ago, when Pliny the Elder recommended poultices of seaweed to treat serious wounds of the limbs, he was in fact presaging marine biotechnology, because the fungi associated with seaweeds have produced antibiotics. We should learn from our elders and take advantage of the capacity to develop marine biotechnology in the United States.

I cannot overemphasize the importance of increasing Federal spending on research and training in the application of molecular biology to the ocean sciences. I urge you to support this bill, and I would be pleased to answer any questions you may have. Thank you.

The prepared statement of Dr. Colwell can be found at the end of the hearing.]

Mr. ORTIZ. Thank you. I would like to remind the witnesses if you could stay within the compliance of five minutes because some of the members have to go to other meetings, and we would like to give them the opportunity to ask questions. Dr. Wilson.

STATEMENT OF SAMUEL H. WILSON, M.D., DIRECTOR, SEALY CENTER FOR MOLECULAR SCIENCE, PROFESSOR, DEPARTMENT OF HUMAN BIOLOGICAL CHEMISTRY AND GENETICS

Dr. WILSON. Thank you, Mr. Chairman and members of the Subcommittee. I am Samuel Wilson of the University of Texas Medical Branch at Galveston. I have been a biomedical research scientist for the past 25 years and spent 24 years of that time on the staff of the National Cancer Institute here in Bethesda before moving to Galveston approximately a year and a half ago.

I am here today to represent the marine biotechnology research group in the Texas-Gulf Coast Region. My testimony will focus in two areas.

First, marine biotechnology ongoing in the Texas-Gulf Coast Region, and secondly in one specific application of biomedical research that is provided by marine biotechnology.

As you have already heard, Mr. Chairman, marine biotechnology has a very wide range of applications. And through the advances of molecular biology, we are now in a unique position to take advantage of this new technology to enhance marine life. And that really is a new position for research scientists at the present time.

One of the most promising and wide ranging techniques in this field is understanding the genetic mechanisms of marine organisms.

This genetic research is generally considered to be one of the most advanced areas in the field of biotechnology, and because of the wealth and the diversity of marine organisms and the unique substances they contain, biotechnology at the molecular level in this area can achieve truly revolutionary advances.

I speak on behalf of a large group of marine biotechnology researchers; at Texas A&M University, at the University of Texas Medical Branch, at Southwest Texas State University, and at M.D. Anderson Cancer Center. Also work at the Institute of Biotechnology at Texas A&M at Houston focuses on marine life.

Collectively, we are in a position to take advantage of this new molecular biology technology, particularly in the area of gene cloning. And thereby, to have a real impact on marine life in the Texas-Gulf Coast Region.

I will now switch to focus on a specific marine biotechnology result that could impact cancer chemotherapy. We live in a world that poses continual threats to our chromosomes and the DNA, the genetic material, therein. As shown on the chart over here to the right (see chart at end of hearing), I have listed how exposure to sunlight (up on the upper right-hand portion), or to toxic chemicals, can eventually cause genetic damage.

Mr. ORTIZ. Is there any way that we can raise that chart a little bit up if it can be done so that other members can see it? That is fine, thank you.

[The chart referred to can be found at the end of the hearing.]

Dr. WILSON. Yes, as shown here, genetic damage (on the right-hand side), is produced after exposure to toxic chemicals in the environment or for example, sunlight. This genetic damage is then subject to what we call DNA-repair (in the yellow box in the middle).

All cells have protein systems for repairing genetic damage (as shown down here in the lower right-hand corner). Also, the cell cycle control systems that determine how fast cells divide have an impact on whether damage to DNA is actually repaired. If the damage is repaired, then the cells return to normal. If it is not repaired, then a specific mutation is introduced into a gene, and this can eventually lead to diseases such as cancer and birth defects.

The general pathway of the transfer of exposure to disease is quite clear in the case of human cancer. Now, what we are proposing to do in the application of fish research to human cancer is to clone the fish genes that are responsible for DNA repair.

Scientists at M.D. Anderson Cancer Center and at Southwest Texas State University have recently shown that several of the DNA-repair genes in fish are virtually identical to the genes that we have in our cells. And, the DNA repair process itself is quite similar in fish and in human cells. Therefore, the fish system is an appropriate system with which to conduct cancer research.

This type of research can be done on a cost-effective basis much more so than we can consider with traditional animal models, and it also can occur at a much faster rate than we see with the traditional animal models. Therefore, we have decided to establish a collaboration, a close working relationship, with marine biotechnology scientists in the State of Texas to conduct genetic studies using the fish/animal model.

Among the practical applications of this research could be in genetically engineering fish, so that they can more efficiently conduct DNA repair. This could have a major impact on their ability to tolerate petrochemicals in the marine environment. One of the most common forms of genetic damage is through DNA alkylation which occurs after exposure to such chemicals as vinyl chloride, other kinds of petrochemical industry products.

Also, the ability to detect genetic damage within key genes in the DNA-repair pathway and in the cell division control pathway can allow us to determine whether, in fact, there are harmful chemicals in the marine environment, which is a very critical question we need to consider in the area of future economic development.

In closing, I repeat that through advances in the field of molecular biology, which is a new science we are beginning to make use of in medical research and in many other areas, as you have heard today, we are now in a position to improve marine life and also to interface this research with improving the health of human beings.

We very strongly support this bill and thank you very much for your efforts in championing it.

[The prepared statement of Dr. Wilson can be found at the end of the hearing.]

Mr. ORTIZ. Thank you, Dr. Wilson. Dr. Ostenso.

STATEMENT OF DR. NED A. OSTENSO, ASSISTANT ADMINISTRATOR FOR OCEANIC AND ATMOSPHERIC RESEARCH, NATIONAL OCEANIC AND ATMOSPHERIC ADMINISTRATION, U.S. DEPARTMENT OF COMMERCE

Dr. OSTENSO. Mr. Chairman, it is always a pleasure to represent NOAA in front of your Subcommittee. I am particularly pleased to be here on this occasion.

I have a long and fact-filled formal presentation that was prepared by Dr. David Attaway, the Marine Biotechnology Program Director in Sea Grant. With your permission I would like to submit that to the record and summarize it.

Mr. ORTIZ. It will be included for the record.

Mr. OSTENSO. It will be a valuable contribution to your deliberations. Let me begin by saying that NOAA supports the intent of this bill under consideration, which would expand marine biotechnology research.

Fully supporting Dr. Colwell's imperative peer review and quality control, we do however have some reservations about setting up a separate competitive review panel for biotechnology proposals. I will get back to that later.

In the meanwhile, I would like to answer the questions of why marine biotechnology and why Sea Grant. Last night I was reading a book entitled "The Great Technology Race, Why We are Losing and What We Need To Do To Compete". The opening statement in this book I thought was particularly relevant to this hearing, and I would like to quote it.

"A wonderful new world is in the process of being born. Geopolitics are being turned upside down. New scientists and technologies will render vast holdings of territory and natural resources almost superfluous. Japan, a country with almost no natural resources, is one of the wealthiest nations of the world; the former Soviet Union, with vast holdings of territory and natural resources, is one of the poorest. We are leaving behind the last vestiges of the industrial age where power belonged to the Nation that could build the world's largest anything. Now we are moving into a hyperdiminutive world of nano-, pico- and femto-, billionth, trillionth and quadrillionth of a meter to a second." He then goes on to develop that new products of the future will be built atom by atom as a raw building materials and similarly services such as delivery of medicine, waste treatment and so forth will be done from the basic building material of nature.

The salient technology he highlights in this book as it goes on is biotechnology, and he goes on to make the point because it is so pioneering and high risk that support of basic research is an appropriate Federal Government responsibility.

Moving on to the question of why marine biotechnology. Most of the major groups of plants, animals and microorgans in the earth are primarily or exclusively marine. In fact, more than 80 percent of all phyla are found only in the sea. So far, researchers have barely begun to explore their products and processes as a basis of biotechnology development.

But as you pointed out in your own opening statement, Mr. Ortiz, that our terrestrial bias is evident in the fact that only one

and a quarter percent of our research funding in biotechnology goes to marine biotechnology.

Unless marine biotechnology is highlighted and singled out for attention, I submit that it will continue to be substantially overlooked considering the biases of our society.

Because environmental conditions in the ocean are so different from those on land, the marine organisms often have unique metabolic capabilities that can be exploited by biotechnology. So not only is the variety there, but there are unique characteristics in this area.

Next topic is why Sea Grant. The very nature of Sea Grant and the way it was put together by Congress nearly 25 years ago was to organize and foster interdisciplinary research. The development of biotechnology often requires interdisciplinary approaches. In fact, I would argue that it is essential.

And even more so the delivery of the fruits of this research is interdisciplinary. Sea Grant is unique in conducting basic and applied academic research overtly geared to providing science and technology and support of commercial development.

Sea Grant recognized the potential importance of marine biotechnology early on and is a primary vehicle for the academic research in this field.

Sea Grant has a unique role in conducting fundamental and applied research in support of aquaculture which is covered under this legislation that we are considering today.

Biotechnology and other molecular sciences, as well as engineering, are critical to aquaculture development and disease and reproductive control, formulation of economic diets, development of recirculating culture systems and genetic improvement of aquaculture species for the production of food, feed and chemical processes.

Sea Grant carries research to application through the formal advisory program and by fostering collaboration and research between academia and industry.

It is for these reasons that we do have reservations about a separate review panel for biotechnology proposals, fearing that this may isolate this body of research from the ongoing body of related natural science going on in the Sea Grant Program, and more significantly it might isolate it from the support of economic, engineering, education and particularly the marine advisory services that are now reviewed as a whole within the Sea Grant Program.

Secondly, we would argue that there are appropriate review mechanisms in place at both the individual project level and at the overall program level to assure the quality control that Dr. Colwell rightly supports.

As an alternative, one might suggest that one or more members of our already legislatively mandated review panel be a person with recognized expertise in marine biotechnology and he, with the community at large, can oversee the preparation of the reports called for.

The responsibility of Sea Grant to maintain a coherent oversight over this program is undeniable, and I would not argue that for a second.

Thank you for the opportunity to testify.

[The prepared statement of Dr. Ostenso can be found at the end of the hearing.]

Mr. ORTIZ. Thank you, Doctor. Now we go to Dr. Chang. Doctor?

**STATEMENT OF DR. JOSEPH Y. CHANG, PRESIDENT AND CEO OF
OSTEOARTHRITIS SCIENCES, INCORPORATED**

Dr CHANG. Thank you, Mr. Chairman, and members of the Subcommittee. I am Joe Chang, President and CEO of Osteoarthritis Sciences, a start-up biotechnology company located in Cambridge, Massachusetts. We are just over a year old and our work force consists of 20 highly trained biotechnology scientists from all across the country.

I am here today to speak in support of the Marine Biotechnology Investment Act of 1993. Historically, a very significant number of useful drugs have been derived from terrestrial sources, aspirin, ephedrine, digitalis and taxol to name a few. There is an even greater promise that the vast marine life in our oceans will provide an even greater abundance of therapeutic drugs and new products. And I am convinced that it is innovative commercial biotechnology companies working close with university scientists that will make this promise a reality.

OsteoArthritis Sciences, Inc., is a new biotechnology company with the mission of commercializing novel drugs for the treatment of osteoarthritis and related-connective tissue diseases. Marine biotechnology constitutes a major component of the company's research efforts and remains a focal point of our drug discovery efforts.

A very major component of our developmental plan is a joint academic industry partnership supported by matching Osteoarthritis Sciences, Inc., funds and grants from the National Sea Grant Program to our university collaborators.

In this program, we have demonstrated that marine organisms are a rich resource of breakthrough drugs that will meet our therapeutic objectives. Working with Drs. Fenical, Faulkner and Jacobs of the University of California Sea Grant Program, we have identified several potent antiinflammatory agents such as pseudopterosins, which we will be evaluating in a variety of inflammatory diseases and developing for commercialization.

Other substances developed in this program are also scheduled for comprehensive preclinical development in the near future. Clearly, the therapeutic value of pseudopterosins would be unrealized without the close academia/industry collaboration established through Sea Grant efforts.

Another aspect of this program is the opportunity to link exciting new concepts in drug discovery with marine biotechnology. Such an example is the recent discovery by the California group of an exciting new drug produced by the cultivation of a marine bacterium under saline fermentation conditions.

This important discovery illustrates the need to develop entirely new coastal industries which explore the development of salt water-based fermentation products. We will be the first industry to patent a discovery from this new technology.

In addition to identifying the above novel antiinflammatory compounds, the company's collaboration with these Sea Grant marine scientists has also uncovered several compounds that retard the destruction of cartilage that occurs in osteoarthritis patients.

The evidence to date suggests that these new marine products would be useful in repairing cartilage and may represent a major breakthrough in the treatment of osteoarthritis.

There is no question that our partnership effort with the Sea Grant scientists has been a major component of our success to date. However, if we are to continue this successful search for new marine-derived drugs, we need to ensure that Federal funding of marine biotechnology within the National Sea Grant College Program network is adequate and to recognize the fact that this emerging leading-edge technology is vulnerable to foreign competition.

Research and development in biotechnology in the U.S. is facing increasing competition from abroad, and this can result in an erosion of our competitive position in marine biotechnology.

In conclusion, I have documented one example in which Sea Grant has played a major role in providing successful technology transfer between academia and industry to commercialize research results. There are many others involving numerous applied aspects of aquaculture, bioremediation and marine product development.

Thank you, Mr. Chairman.

[The prepared statement of Dr. Chang can be found at the end of the hearing.]

Mr. ORTIZ. Thank you, Dr. Chang. Dr. Koskan.

STATEMENT OF DR. LAWRENCE P. KOSKAN, PRESIDENT, DONLAR CORPORATION

Dr. KOSKAN. Mr. Chairman and members of the Subcommittee, I am pleased to be here today to testify on behalf of the importance of Federal involvement and investment and enhancement of the United States marine biotechnology industry.

My name is Larry Koskan and I am President of Donlar Corporation which is located in Bedford Park, Illinois. The purpose of my testimony is to convey to you that industry-government-university partnerships are critical to realizing the potential of marine biotechnology in support of enhanced U.S. economic competitiveness and jobs creation.

Breakthroughs in the development of new technologies based on natural models may also result in products that are safe and environmentally friendly. My company serves as a good illustration.

There is increasing pressure on industry to be considered green as part of its overall image and corporate culture. Industries involved in the manufacture and sale of chemical products for consumer or industrial markets are particularly sensitive to this pressure.

Many key industrial chemicals used extensively throughout the world are now being reexamined due primarily to their lack of biodegradability and unknown fate in the environment.

Donlar Corporation was formed on January 8, 1990, with the goal of manufacturing and marketing a biodegradable protein

known as polyaspartate to address the need for nonpolluting, non-toxic and environmentally safe water-soluble polymers.

By 1993, Donlar had developed several patents covering processes, composition and end use of polyaspartate that together have the potential to replace at least one billion pounds of nonbiodegradable chemicals sold worldwide annually.

The original idea which led me to form Donlar arose from my initial contact with two Sea Grant marine biologists, Dr. A. P. Wheeler at Clemson University and Dr. C. S. Sikes at the University of South Alabama.

Drs. Wheeler and Sikes initiated their work in 1981, with funding from the National Science Foundation and the National Sea Grant College Program, where they determined that biopolymers found in oyster shells contain proteins that mimic the performance of certain synthetic polymers known as polyacrylates.

Polyacrylates are produced by industry in the hundreds of millions of pounds, and are found in many consumer and industrial products. They have a well-defined market and are currently considered the most cost-effective product in their class.

As examples, polyacrylates have become a key ingredient in water treatment products, detergents and cleaners, paints and coatings, household and personal care products, baby diapers, waste treatment and oil production to name a few.

Although polyacrylates represent the key ingredient, they are nonbiodegradable, and they accumulate in the environment.

Initially, very few industries showed interest in this new technology. Having worked for the world's largest water treatment company as Vice-President of Research of Water and Waste Treatment, I recognized the potential and the benefits of polyaspartate as presented by Drs. Wheeler and Sikes.

Developing seed money, I was able to hire two chemists and a chemical engineer to help develop the methods to produce polyaspartate in commercial quantities. Within a few months, we received our first patent for the first commercial process to manufacture polyaspartate.

Because our resources were extremely limited, Donlar relied heavily upon the services and help of Sea Grant research, particularly those of Dr. Wheeler and his staff at Clemson University. They supplied analyses and confirmed activity data for patent applications and sales information.

In addition, the Chemical Engineering Department at Clemson helped develop some of the engineering and process specifications that helped make the process practical.

As a result of this industry-government-university partnership, additional needs and opportunities for collaborative research have been identified. Donlar and Clemson University entered into a joint development agreement in which Donlar and Sea Grant are supporting research for the continued development of this technology.

The agreement allows Clemson to own the patents of all cooperatively developed technology while Donlar retains right of first refusal to practice and commercialize the technology.

Working with Gilbraith Labs in Knoxville, Tennessee, continued research of polyaspartates has led to the surprising discovery of a new series of environmentally safe agriculture products. They have

been found to enhance plant efficiency by optimizing the uptake of fertilizers and micronutrients required to sustain plant growth and give improved yields.

An unexpected result of this application is that uptake efficiencies are so high that at least a 50 percent reduction in the use of fertilizers is easily achieved. Since less fertilizer is used, a significant reduction of pollution runoff is gained.

By many practical and promising uses from this technology transfer can and are being found. As a result of the development of technology derived from Sea Grant research on oyster shell proteins.

We have recently introduced this technology on a global scale. We hope to commercialize it in the U.S. in a timely fashion in order to seize upon the opportunity before foreign interests do, as their environmental pressures are greater.

In order to maintain Donlar's competitive lead and continue our growth, four more people were hired, and we recently moved into an improved facility operated by the Illinois Institute of Technology.

We support the bill to establish a marine biotechnology program within the National Sea Grant College Program. We have benefited from the Sea Grant support that was awarded to Dr. Wheeler and Clemson University.

It is obvious that Sea Grant funding at Clemson aided in the technology transfer of critical information to Donlar. That transfer has allowed Donlar to bring in additional capital.

The proposed bill mirrors our progress in that we have created jobs, produced products that will provide significant environmental benefits, developed the leadership role in the United States for this technology, and initiated a return on investment for the taxpayers by providing additional support to the university program. Thank you.

[The prepared statement of Mr. Koskan can be found at the end of the hearing.]

Mr. ORTIZ. Thank you very much. There is no question that this hearing this morning has been very interesting and quite educational. I think most of us have learned a lot this morning.

To all the witnesses, I have a question now. I believe that each of you has been able to see a draft of Chairman Studds' bill which was introduced yesterday. I first want to ask each of you for your comments on this legislation and any improvements or changes that you recommend. Anybody that can start off and then we will follow through.

Dr. BURRIS. I think that as written it is a very good piece of legislation. I am very comfortable with the establishment of a separate review panel within Sea Grant for this, and in fact, I would speak strongly for that and would view that as an important part of the bill.

I might quibble with the definition of marine biotechnology and might broaden that slightly, but I think overall it is a very fine piece of legislation.

Mr. ORTIZ. Thank you.

Dr. COLWELL. I support the bill in its present form. Again, there is no sense doing any small wordcrafting. I think if we were able to

have this bill enacted, we would be a dozen leagues ahead of ourselves. Thank you.

Mr. ORTIZ. Thank you, Dr. Colwell.

Dr. WILSON. We have some prepared recommendations that I would just like to read. Concerning the bill, we believe it is good that the bill reserves money outside the college level, and it is very good that the bill puts review at the national level. A point we strongly emphasize is that a local review process cannot bring the appropriate expertise to the subject matter.

It should be clearly stated in the bill that funding is for investigator-initiated applications. This will ensure the best scientific productivity and facility and the selections can be done through the time-tested and effective peer review process, as is conducted with most NIH-funded research, for example.

Emphasis should be placed at the basic science level. That is, the discovery and isolation of necessary molecular tools and on the developmental phases, such as transgenic technology.

Application trials, growouts, et cetera, should revert to other grant opportunities. Thus, the bill should allow the development of molecular tools for ecological studies as valid new products, but exclude the application of already matured technologies, such as genetic stock, assessments and so forth, since these technologies have already been adapted for use by other State and Federal agencies.

Wording of the bill is important in this particular area, because we don't want to exclude the development of new technologies for exactly the purpose that we have been discussing today.

Finally, we recommend considering a longer grant cycle for the program. Sea Grant normally operates on a two-year cycle. This is not long enough for reasonable progress in molecular biotechnology start-up projects, and therefore three to five years would be better. Thank you.

Mr. ORTIZ. Thank you.

Dr. OSTENSO. I would like to readdress my already referred to concern. One of the unique things about the Sea Grant Program is that it is an agency to institution approach to support of research, rather than an agency to principal investigator. It is because of this I would submit that history will look back and find that the Sea Grant Program was the agency most salient in the origin of marine biotechnology because it was an effort for interdisciplinary people to work together in a coherent way in a topic that wasn't popular at the time.

I do have concern over a separate review process that might serve to 'ghettoize', if you will, marine biotechnology research from other relevant areas of not only research but activities that are existent within the Sea Grant Program.

I am pleased at the many complimentary things that have been said about Sea Grant in general, and the Sea Grant marine biotechnology program in particular by my fellow witnesses. And it is because of that, that I am concerned about setting aside a separate management process for marine biotechnology research.

We do have a well-defined, an assiduously followed review process at the individual project level and at the program level, and I think that would be sufficient to maintain the intellectual integrity

of this effort while not isolating it from the other Sea Grant activities. Thank you.

Mr. ORTIZ. Dr. Chang.

Dr. CHANG. I believe the Investment Act as it is being written is excellent. Perhaps the emphasis should be slanted toward academia because when products come through, industrial biotechnology companies such as ourselves, would be able to seek the funds to develop those compounds.

I agree with Dr. Sealy that the basic research ought to be emphasized in this particular Act and as we study the molecular mechanisms involved in marine organisms life, it would provide a lot of insights into how diseases can be managed and in the clinical population. Thank you.

Mr. ORTIZ. Thank you. Dr. Koskan.

Dr. KOSKAN. Thank you. As Dr. Colwell stated, we are a small company and developing capital resources to go into commercial mode is quite extensive and arduous at best.

What I would like to see in the bill is incentives that allow commercialization on a small level to proceed. As far as companies like myself and Dr. Chang are concerned, I think they would represent a more rapid spinoff in development of the technology base.

What we would like to see is incentives in the bill for universities to allocate the funds on a priority basis so that technology transfer to small companies can be facilitated.

We would like the bill to provide small companies with sales less than one million dollars to receive matching funds as a result of the technology transfer.

We would like the bill to provide funds up to two million dollars for small companies receiving technology to build demonstration pilot plants in order to prove commercialization.

The bill should also provide provisions for reinvestment of the granted funds used by the companies back to universities to spawn continued and mutual growth.

The result of these additions to the bill will encourage a more rapid development and spinoff of technology as I said, so that new and stable jobs can be created. Marine science can be developed as a renewable resource for a wide variety of new and safe products and the environment can be improved and replenished. Thank you very much.

Mr. ORTIZ. Thank you. I do have another question before I yield to my good friend and colleague from Texas. There has been an enormous Federal investment in the biotech field with many, many remarkable advancements. To what extent are the advances in nonmarine areas applicable to marine biotech, and are these techniques readily transferred. Specifically, are there particular scientific advances that might only be obtainable through marine biotech, and if so, why? Anyone that might want to answer that question?

Dr. COLWELL. I think that the advances that have been made in other areas are absolutely and eminently transferable. One point that must be made is that we are now able to exploit the marine environment in an environmentally protective way. We need no longer harvest every single sea urchin that may have the compound that may treat cancer. All we need to do is clone the genes,

reproduce them in the laboratory, and produce the material in the laboratory, leaving the sea urchins where they belong in the environment. And I think that is a very critical and important advance that allows us then to use the resources of the oceans—three-quarters of the earth's surface—that we have not really been able to draw on in the past.

Mr. ORTIZ. Very good. Anyone else? Dr. Wilson.

Dr. WILSON. One comment I would make is that in just the past few months information has emerged that genes cloned in other systems, bacterial systems to human, in fact, are very similar to the corresponding genes in fish. Therefore, genes isolated from various other systems can be used as templates for application of the molecular cloning technology to the fish system.

In the case that I just alluded to of a DNA-repair enzyme, it is remarkable that the sequence of this protein is 90 percent identical with the sequence of the protein in humans. And, even the structure of the fish gene itself, a very complex genetic unit, is virtually the same as the gene in our bodies. This really is a new and inspiring insight in the field, and shows that direct transfer of this molecular technology to marine and fish life is perfectly straightforward.

One other comment that I might make in this area of transfer of technology, concerns the technology of transgenic animals, the science of genetically altering animals strategically to enhance their ability to deal with the environment or with living. This technology, which has been worked out with mice and with other organisms, recently has been transferred successfully to fish. And in fact, with some species of fish, the use of transgenic technology may prove to be substantially easier, faster, and simpler than it is with the mouse-model system.

Mr. ORTIZ. Dr. Burris.

Dr. BURRIS. What one sees in science is that there is clear movement of information, techniques, back and forth between the marine and terrestrial environment. To this point, the main movement, as you have already alluded to, is from the terrestrial to the marine, but I would point out that as we explore new and novel systems in the marine environment, one would hope that the flow would increase not only within the marine environment and marine biotech, but also to terrestrial systems.

One can cite in the past clear examples of where marine models have served us very well in the biomedical field. Much of the work that we know about in transmission, nerve transmission, was done originally using the axon, the main nerve cord in squid, and continues to be one of the primary models. So here we have an example of the marine organism being used and applied to higher organisms.

At the MBL we have a group of researchers who work on toad fish. They use toad fish for diabetes research because the islets of Langerhans are the cells where insulin is produced are consolidated in the pancreas of the toad fish making them easier to work on.

We use the rectal glands of sharks for research in cystic fibrosis because they make a beautiful model for chloride secreting cells. Traditionally, there has always been some marine movement into the terrestrial, where the models were appropriate, and I see this

as stimulating and opening up all of biotechnology in its applications to a world that has been little utilized up to this point.

Mr. ORTIZ. Dr. Colwell.

Dr. COLWELL. I would like to add that marine systems have already revolutionized the medical diagnostic arena in the PCR, the polymerase chain reaction, which has allowed detection of genes even when present in one or two molecules. And that is the use of the polymerase from hydrothermal vents.

Two of our scientists, Dr. Frank Robb, and Dr. Dan Stein, have isolated some of the polymerases' enzymes from hydrothermal vent organisms, which live at very high temperatures in the deep sea under high pressure. They have provided new impetus to the polymerase chain reaction.

Mr. ORTIZ. Thank you. At this time, if we don't have any other response to that question, I would like to yield to my good friend and colleague and the Vice-Chair of this Subcommittee, Mr. Green, to see if he has got any questions.

Mr. GREEN. Thank you, Mr. Chairman. Just a couple of short questions and I think any one of the panel could answer this one. Because I know in your opening statement you talked about how much compared to Japan we spend, but I would like to see if some of the panelists know the amount say that other countries spend on marine biotechnology as compared to what the United States does.

Dr. COLWELL. I just returned from Norway, which has built a new laboratory. Norway, Sweden and Denmark have made major investments in biotechnology, and I would estimate that it is probably in the range of \$50 million to \$100 million. Those countries are relatively small compared with the United States. But in Norway, Hydro Norsk, the largest multimillion dollar company, is making a major investment in the fisheries, which are, of course, very important to the Scandinavian countries and to Norway.

I would also point out that Taiwan has made a multimillion-dollar investment in fisheries because of the shrimp harvest, which is very important. Even countries like Ecuador, whose shrimp marine culture industry is worth \$400 million—40 percent of the gross national product of that country—are making major investments in marine biotechnology.

Dr. KOSKAN. I would like to make a comment to that. I can't give you any numbers as to what—how much money is being spent on marine biotechnology per se, but I can give you a feel for the commercialization side of the ledger. And since we introduced this technology three years ago, we have found that there are probably ten times more research activity by foreign companies in the commercialization of environmentally safe materials based on this technology, and it is being done in Europe, especially in Germany and Japan, than it is in the United States. So I think the feeling is, is that there probably a lot more that is being spent there and it is being realized on the commercial side as well.

Mr. GREEN. Thank you. One last thing and because of the opening statements, particularly from the ranking minority member and Congressman Weldon, under this Act, how would marine biotechnology proposals compete with other funding particularly the Sea Grant proposals, the current funding for Sea Grant?

Dr. OSTENSO. As I believe it was Dr. Colwell pointed out in her statement that the—no, I think it was the Chairman's comments that funding for Sea Grant today is about equal to what it was in 1979 or '80, which means it is about half the effective spending power. Despite this, I think we—Sea Grant as an institution has been particularly protective of marine biotechnology. We haven't been able to exploit all the opportunities that have been presented to us, but biotechnology has prospered relative to other programs we considered of lesser priority.

If I could just add one thing. This wasn't a command decision that was made by me in isolation. It reflects the excellent program leadership we have had within the office and the commitment of the research community, both collectively and individually supporting the highest quality proposals.

Dr. BURRIS. May I just, to put things in context in reference to Mr. Green's question about expenditures. Lots of numbers of course are brooded about as to how much companies and countries spend. The \$200 million dollar figure that I cited relative to Japan is for one specific targeted initiative that media is undertaking presently. Other numbers that I have seen quoted, in fact in a Sea Grant publication on marine biotechnology, put the number in the neighborhood of \$900 million to \$1 billion dollars that the Japanese are spending. So the \$200 million was a targeted initiative just in setting up these two new institutes. But overall, we are talking about approaching a billion dollars that the Japanese are estimated to spend privately and in Federal funding. That gives you a little bit better context of what we are talking about.

Dr. COLWELL. Those data are correct from our study of the industry.

Mr. ORTIZ. Thank you. I have one more question. Are there any dangers in biotechnology development for the marine environment? What steps could be taken to address dangers to the marine environment? Dr. Colwell.

Dr. COLWELL. I think that we need to proceed as we are, carefully and with precautions. Let me give you an example. The antifreeze gene—that is the gene that is present in fish that live in the Antarctic—is triggered when the temperature drops very low. This protein is released into the blood of the fish and allows it to withstand very, very low temperatures.

That gene has been cloned, and it can be introduced into, let us say, striped bass. This would allow a striped bass then to migrate further north, perhaps to Labrador instead of stopping somewhere around Rhode Island. We may say this would be excellent because the fish would come back bigger and fatter, and there would be more fun for the sports fishery and benefits for the commercial fishery. But there is a question that we have to answer. Will they be feeding on the food that the other species of fish in the Labrador region feed on? Would that upset the ecological balance?

We have to answer these questions, and I think the funding that is requested would allow us to do the kinds of studies that should be done, in tandem with the cloning and genetic manipulation research. So, yes, we should—but I believe that we will find that the threats are minimal, if present at all. And I doubt that they are present. In fact, no recorded case of an untoward event has oc-

curred in all the time—in the last 20 or 30 years— that molecular biology research has been going on.

Nevertheless, it is wise and prudent to move carefully in the release of organisms to the environment.

Mr. ORTIZ. Thank you. Anybody else? If not, let me say that we will share your testimony with the other members of the Subcommittee who couldn't be with us today. This will conclude the testimony for this panel.

I want to thank each and every one of you for your valuable testimony and insight you have shared with us today. And I really think that this hearing serves as an important step in creating an awareness of the importance of marine biotech and the possible impact that this research can have both scientifically and economically. And for this member, I can assure you that this has been a learning experience. I have learned a lot this morning and I hope that I can take time again and read through all your testimony that you have submitted this morning.

Now, if anybody has a statement before we adjourn, feel free to do so at this time. My good friend, Mr. Green? Thank you again for being with us this morning. The meeting is adjourned.

[Whereupon, at 11:20 a.m., the Subcommittee was adjourned, and the following was submitted for the record:]

WRITTEN TESTIMONY

by

Mr. Larry P. Koskan
President
Donlar Corporation
Bedford Park, IL

on

MARINE BIOTECHNOLOGY AND THE
MARINE BIOTECHNOLOGY INVESTMENT ACT OF 1993

BEFORE THE

SUBCOMMITTEE ON OCEANOGRAPHY, GULF OF MEXICO AND
THE OUTER CONTINENTAL SHELF
HOUSE COMMITTEE ON MERCHANT MARINE AND FISHERIES

APRIL 29, 1993

Mr. Chairman and members of the subcommittee, I am pleased to be here today to testify on behalf of the importance of federal involvement and investment in the development and enhancement of the United States marine biotechnology industry. My name is Larry P. Koskan, and I am President of Donlar Corporation which is located in Bedford Park, Illinois, just outside of Chicago.

The purpose of my testimony is to convey to you that industry-government-university partnerships are critical to realizing the potential of marine biotechnology in support of enhanced U.S. economic competitiveness and jobs creation. Breakthroughs in the development of new technologies based on "natural" models may also result in products that are safe and environmentally friendly. My company serves as a good illustration.

There is increasing pressure on industry to be considered "green" as part of its overall image and corporate culture. Industries involved in the manufacture and sale of chemical products for consumer or industrial markets are particularly sensitive to this pressure. Many key industrial chemicals used extensively throughout the world are now being re-examined due primarily to their lack of biodegradability and unknown fate in the environment.

Donlar Corporation was formed on January 8, 1990 with the goal of manufacturing and marketing a biodegradable protein known as polyaspartate to address the need for non-polluting, non-toxic and environmentally safe water-soluble polymers. By 1993, Donlar

had developed several patents covering processes, composition and end use of polyaspartate that together have the potential to replace at least one billion pounds of non-biodegradable chemicals sold worldwide annually. Although we have only sold small quantities to date, we have developed name recognition, an identifiable market niche and educated thousands as to the potential of such a commercially available chemical.

The original idea which led me to form Donlar arose from my initial contact with two Sea Grant marine biologists, Dr. A.P. Wheeler at Clemson University and Dr. C.S. Sikes at the University of South Alabama. Drs. Wheeler and Sikes initiated their work in 1981, with funding from the National Science Foundation and the National Sea Grant College Program, where they determined that biopolymers (a particular class of proteins) found in oyster shells contain proteins that mimic the activity of certain synthetic polymers produced today by industry in the hundreds of millions of pounds. Six patents have been received by the universities for this technology.

These man-made polymers are collectively known as polyacrylates and are found in many consumer and industrial products. They have a well-defined market and are currently considered the most cost-effective product in their class. For instance, polyacrylates have become a key ingredient in:

- * water treatment products to reduce scaling and corrosion in pipes and heat exchange equipment in nearly every manufacturing plant in the world;

* detergents, as an ingredient to keep soil particles suspended in the wash water so they don't reattach to clothing;

* paints and coatings, to keep pigments suspended so paint spreads easily and uniformly; and

* baby diapers, as cross-linked superabsorbents that readily soak up urine and other body fluids.

Although polyacrylates represent the key ingredient, they are non-biodegradable and accumulate in the environment.

Initially, very few industries showed interest in this new technology. Having worked for the world's largest water treatment company as Vice-President of Research of Water and Waste Treatment, I recognized the potential and the benefits of polyaspartate as presented by Drs. Wheeler and Sikes.

Using seed money, I was able to hire two chemists and a chemical engineer to help develop the methods to produce polyaspartate in commercial quantities. Our company moved into an incubator facility in south suburban Chicago and, within a few months, we received a patent for the first commercial process to manufacture polyaspartate. Because our resources were extremely limited, Donlar relied heavily upon the services and help of Sea Grant research, particularly those of Dr. Wheeler and his staff at Clemson University. They supplied analyses and confirmed activity data for patent applications and sales information. In addition, Dr. C. Gooding from the Chemical Engineering Department at Clemson helped develop, with Sea Grant support, some of the engineering and process specifications for a crucial part of the manufacturing procedure that made the process practical.

As a result of this industry-government-university partnership, additional needs and opportunities for collaborative research have been identified. Donlar and Clemson University have entered into a joint development agreement in which Donlar and Sea Grant are supporting research for the continued development of technology. The agreement allows Clemson to own the patents of all cooperatively developed technology while Donlar retains right of first refusal to practice and commercialize the technology. Collaborative efforts to develop superabsorbent polymers and study biodegradation of these synthetic polymers are planned for the near future.

Of special significance is that continued exploitation of the original discovery has led to the development of a new series of environmentally safe agricultural products. They are designed to enhance plant efficiency by optimizing the uptake of fertilizers and micronutrients required to sustain plant growth and give improved yields. An unexpected result of this application is that uptake efficiencies are so high that at least a 50 percent reduction in the use of fertilizers is achieved. Since less fertilizer is used, a significant reduction of pollution runoff is gained. Many practical and promising applications from this technology transfer can and are being found as a result of the development of technology developed from Sea Grant research on oyster shell proteins.

We have recently introduced this technology on a global scale; we intend to commercialize it in the U.S. in a timely fashion to seize upon the opportunity before foreign interests

do. In order to maintain Donlar's competitive lead and continue our growth, four more people were hired, and we recently moved into a improved facility with pilot plant capability owned by the Illinois Institute of Technology.

We support the bill to establish a marine biotechnology program within the National Sea Grant College Program. We have benefited from the Sea Grant support that was awarded to Dr. Wheeler and Clemson University. It is obvious that Sea Grant funding at Clemson aided in the technology transfer of critical information to Donlar. That transfer has allowed Donlar to bring in additional capital. The proposed bill mirrors our progress in that we have created jobs, provided products from the technology that has significant environmental benefits, developed the leadership role in the United States for this technology and initiated a return on investment for the taxpayers by providing additional support to the university program.



OsteoArthritis SCIENCES, INC.

Mr. Chairman and members of the Subcommittee.

I am Dr. Joseph Y. Chang, President and C.E.O. of OsteoArthritis Sciences, Inc., a start-up biotechnology company located in Cambridge, Massachusetts. We are just over a year old and our workforce consists of twenty highly trained biotechnology scientists from all across the country. I am here today to speak in support of the Marine Biotechnology Investment Act of 1993.

Historically, a very significant number of useful drugs have been derived from terrestrial sources: aspirin, ephedrine, digitalis and taxol to name a few. There is an even greater promise that the vast marine life in our oceans will provide an even greater abundance of therapeutic drugs and new products. And I am convinced that it is innovative commercial biotechnology companies working close with university scientists that will make this promise a reality.

OsteoArthritis Sciences, Inc. is a new biotechnology company with the mission of commercializing novel drugs for the treatment of osteoarthritis and related connective tissue diseases. Marine biotechnology constitutes a major component of the company's research efforts and remains a focal point of our drug discovery efforts.

A very major component of our developmental plan is a joint academic-industry partnership supported by matching OsteoArthritis Sciences, Inc. funds and grants from the National Sea Grant Program to our university collaborators.

In this program, we have demonstrated that marine organisms are a rich resource of breakthrough drugs that will meet our therapeutic objectives. Working with Drs. Fenical, Faulkner and Jacobs of the University of California Sea Grant Program, we have identified several potent anti-inflammatory agents, such as pseudopterosins, which we will be evaluating in a variety of inflammatory diseases and developing for commercialization. Other substances developed in this program are also scheduled for comprehensive pre-clinical development in the near future. Clearly, the therapeutic value of pseudopterosins would be unrealized without the close academia-industry collaboration established through Sea Grant efforts.

Another aspect of this program is the opportunity to link exciting new concepts in drug discovery with marine biotechnology. Such an example is the recent discovery by the California group, of an exciting new drug produced by the cultivation of a marine bacterium under saline fermentation conditions. This important discovery illustrates the need to develop entirely new coastal industries which explore the development of salt-water based fermentation products. We will be the first industry to patent a discovery from this new technology.

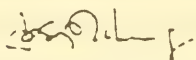
In addition to identifying the above novel anti-inflammatory compounds, the company's collaboration with these Sea Grant marine scientists has also uncovered several compounds that retard the destruction of cartilage that occurs in osteoarthritis patients. The evidence to date suggests that these new marine products would be useful in repairing cartilage and may represent a major breakthrough in the treatment of osteoarthritis.

There is no question that our partnership effort with the Sea Grant scientists has been a major component of our success to date. However, if we are to continue this successful search for new marine-derived drugs, we need to ensure that federal funding of marine biotechnology within the National Sea Grant College Program network is adequate and to recognize the fact that this emerging leading edge technology is vulnerable to foreign competition. Research and development in biotechnology in the U.S. is facing increasing competition from abroad and this can result in an erosion of our competitive position in marine biotechnology.

In conclusion, I have documented one example in which Sea Grant has played a major role in providing successful technology transfer between academia and industry to commercialize research results. There are many others involving numerous applied aspects of aquaculture, bioremediation and marine product development.

Given the potential of the oceans as a resource for new product discovery, and the effectiveness of the Sea Grant Program in making successful commercial linkages, there is no question that the new bill before you will underwrite the establishment of new technologies and viable new industries based upon applied marine research.

It is widely accepted that Marine Biotechnology is among the most important of the new emerging technologies in the United States. With continued leadership and support of the Congress through groundbreaking legislation such as this Investment Act, there is no question that marine biotechnology will contribute significantly to the next decade's industrial processes, products, and job base. For these reasons, I am an enthusiastic supporter of the MBI Act.



Dr. Joseph Y. Chang
President and C.E.O.



OsteoArthritis
SCIENCES, INC.

To: Mr. Chris Mann
U.S. House of Representatives
Committee on Merchant Marine and Fisheries
Room 1334, Longworth House Office Building
Washington, DC 20515-6230
Fax: (202) 226-3324 Phone: (202) 225-6747

From: Patrice Bottari for Dr. Joseph Y. Chang
OsteoArthritis Sciences, Inc.
Fax: (617) 252-9096 Phone: (617) 252-6886

CC:

Date: May 28, 1993

Pages: 7

Re: Attached Responses

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ONE KENDALL SQUARE, BUILDING 200
CAMBRIDGE, MASSACHUSETTS 02139
617.252.6886 TEL 617.252.9096 FAX

Dr. Joseph Chang:

- 1) Is increased federal investment needed to maintain U.S. competitiveness in marine biotechnology?
- 2) In what areas of research, development, technology transfer, and education is this investment most needed?
- 3) How can partnerships in marine biotechnology among government, industry and academia be best promoted?
- 4) What insights can biotechnology provide into ecological and evolutionary problems and how can these lead to better resource management?
- 5) What are the dangers of biotechnology development for the marine environment? What steps could or should be taken to address these?
- 6) What promise does marine biotechnology hold for enhancing the following areas of research and industry: aquaculture; bioremediation; seafood product safety; pharmaceuticals; polymers and lubricants?
- 7) How would additional support from Sea Grant have made development of your products easier or quicker?
- 8) At what stage of developing a marine product is government support most critical?
- 9) Besides research, how else could Sea Grant assist in getting marine products to market?

Sea Grant made it interesting.



OsteoArthritis SCIENCES, INC.

Is increased federal investment needed to maintain U.S. competitiveness in marine biotechnology?

1. An increased federal investment is needed to maintain U.S. competitiveness in marine biotechnology. Over the last decade or so it has become increasingly evident from biological, pharmacological and chemical investigations by American, European and Asian scientists that the potential resource for the development of new products from marine life through biotechnology is very real. Scientific groups on several countries including France, Germany, India, China, Japan and the United States have organized groups whose focus currently is on the discovery and development of biomedical applications of marine natural products. The United States has led the way in this activity and several marine natural products are currently in clinical trial or are being evaluated for that purpose. Early investigations were focused around classical approaches involving development of products such as agar, food supplements for agriculture, resins, antibiotics at the basic research level. Methods were developed for reliably analyzing the ecological consequences of human population activities such as energy development, pesticide use and a whole host of associated commercial activities. With the development of marine biotechnologies in recent years, an increase in federal funding will only lead to further discoveries that will benefit mankind.

More recent investigations of fundamental biological processes such as cell replication, nerve conduction, nervous system communication have led to a major understanding of processes such as growth, reproduction and cell-cell interactions. The advances in marine biotechnology have offered the unprecedented opportunity to develop new avenues and models of human disease processes not previously directly accessible for study. The use of animal models such as the white rat, mouse or guinea pig is being supplemented by cell cultures in which the DNA containing elements of a human process have been cloned and expressed through recombinant DNA into primordial cells (marine bacteria, yeast, marine eggs and other replicating cells). These cells are grown in abundance under controlled conditions and human hormones, enzymes and receptors (all parts of a disease process) can now be readily studied and utilized for the design of new types of drug therapy. These human enzymes, hormones and receptors are extremely rare and not accessible to study except through biotechnology. Marine natural products are being studied since they represent the primordial genetic model or template of a future drug and as such are the most rational resource for scientists to turn to, to discover new unique drugs that can affect a disease process in a unique way.

We fully expect to discover new marine natural products that can be used to mitigate even eliminate the effects of certain disease processes associated with arthritis, inflammation, tissue infections, and bone and connective tissue diseases.

A joint federal investment between academic researchers, the biotechnology industry and the Sea Grant program is of great importance to commercialize these potentially breakthrough products. It is imperative that Sea Grant be given the opportunity to capitalize on its success and receive sufficient funding to maintain and excel in its unique mission.

In what areas of research, development, technology transfer, and education is this investment most needed?

2. In our view, the priority areas of research and development should emphasize biomedical applications. The reason for increased investment in medical applications centers around these issues. First, this area of product development is the current focus of several of our leading U.S. biotechnology companies and is of great interest to venture capital investors. These investors provide much of the start up costs for new companies such as OsteoArthritis Sciences, Inc. (OSI) and in large part create the capital which is utilized to build a scientifically relevant research infrastructure committed to new medical applications. It should be noted also that these new companies are providing major job opportunities for young scientists. In fact, the number of new positions available in the biotechnology industry currently exceeds the number of new positions available in conventional drug companies. Many skilled academic scientists have also joined biotechnology companies in order to participate in this dynamic growth. Second, in addition to creating new markets, new employment and new commerce, these companies have an enormous opportunity to provide relief from pain and suffering of many of our people. Focusing on specific medical applications as part of the marine biotechnology program will assure continuing leadership in this field. Third, cost of a drug is largely determined by availability or the cost of syntheses. Patentability of the native or primordial marine natural products, its closely related analogs and the operation of derivatives will require maximum interaction and effort by chemists in which the university scientist can play an extremely important role. This is particularly true with new biotechnology companies in which the number of scientific employees may be less than 100. The chemistry faculty of Universities where they find it appropriate, can look to new and challenging research opportunities by bringing their substantial talents to begin and to open new avenues of investigation and in the long run helps to reduce the costs of medical care. Synthesis and biosynthesis are the key to successful marine natural product development. Providing an inexpensive readily available resource is the key to keeping costs under control.

Technology transfer is a special area of expertise in which Sea Grant has already played a major role. The infrastructure for developing patents transferring information to the biotechnology industry and its review and licensing procedures are currently in place. There is however a great need to improve and streamline the process to the extent that it better serves the needs of the investors and the industry. This is a vital activity needed to assure ample time for research and development to occur and to protect the product during the early stages of development and marketing.

There is a need for a model system to be developed to enhance interaction between the University, their inventors and the biotechnology company. Currently priorities, interests and resources make it difficult for Universities to invest heavily in developing strong patent positions. In addition, the University mission is primarily committed to education. Teaching and education must always come first. Thus, patents and technology transfer are generally considered public service functions by Universities. Resources therefore for patents constitute a problem. Perhaps there could be a government role in assisting with patent costs, although this may be difficult to manage. Probably the major costs of patents should reside with the biotechnology company and government should provide an incentive for efficient interaction between Sea Grant institutions and industry.

With respect to education, the number of natural product chemists with advanced degrees who focus on marine research in the U.S. is currently less than 100. Most are academic scientists distributed throughout the United States. There are fewer than 20 pharmacologists and biologists who focus their research on marine pharmacology. The situation must be significantly improved to maintain our competitiveness in the emerging technology.

How can partnerships in marine biotechnology among government, industry and academia be best promoted?

3. The best way to promote partnership between industry, academia and the government is to expand the current Sea Grant program. Sea Grant already has in place an extensive network of industry relationships. This includes almost all the major pharmaceutical companies along with elements of the emerging biotechnology interest. In addition, they are well established in the fisheries and agriculture industries. Provisions have already been made through matching fund requirements to encourage academics to seek and establish relationship with industrial partners and to encourage technology transfer.

Currently it is estimated that there are about 80 companies directly or indirectly associated with the Sea Grant network. The number of biotechnology companies involved is rising rapidly and with government funding of Sea Grant a major increase is expected to occur.

What insights can biotechnology provide into ecological and evolutionary problems, and how can these lead to better resource management?

4. This question is maybe more appropriate to problems in agriculture than in medical applications. The resource management problems associated with delivery of a marine natural product are substantial and should stimulate considerable effort in the area of intermediate biosynthesis. This can be predicted to be accomplished through isolation and characterization of key rate limiting enzymes involved in the biosynthesis of natural product precursors leading to synthesis of the final drug. Once the enzymes are isolated then they are expressed in bacteria or yeast through application of biotechnology for the production of the products. The cost of the product is reduced and the ecological pressure eliminated.

There are examples of this practice already in place. For example, the production of prostaglandins from harvesting a soft coral to the chemical synthesis of these drugs was successfully carried out by Nobel laureate E.J. Corey at Harvard University. More recently, simple analogs of the antiinflammatory drug manolide have been synthesized and they are currently in clinical trial. Thus, for economic reasons alone, marine derived products will most likely be synthesized in the laboratory for commercialization.

What are the dangers of biotechnology development for the marine environment? What steps could or should be taken to address these?

5. The dangers to the marine environment can result from over exploitation or excessive harvesting. This may not directly result from the activities of the biotechnology company but may result as a consequence of secondary markets initiated by unregulated industries.

Ecological studies and investigations of harvesting techniques during the early stages of market development will provide added insight into correct resource management. For example, studies have been proposed where by 8-10ft. segments of PVC piping are located below water at specified locations. At specified time the pipes are brought to the surface, the growth of the organisms measured, and segments or branches harvested. Once a colony is established, then the need for harvesting wild organisms becomes relatively unnecessary. Such studies can serve as the major resource for a natural product during the early stages.

What promise does marine biotechnology hold for enhancing the following areas of research and industry: aquaculture; bioremediation; seafood product safety; pharmaceuticals; polymers and lubricants?

6. Historically, a very significant number of useful drugs have been derived from terrestrial sources: aspirin, ephedrine, digitalis and taxol to name a few. There is an even greater promise that the vast marine life in our oceans will provide an even greater abundance of therapeutic drugs and new products. And I am convinced that it is innovative commercial biotechnology companies working close with university scientists that will make this promise a reality.

OsteoArthritis Sciences, Inc. is a new biotechnology company with the mission of commercializing novel drugs for the treatment of osteoarthritis and related connective tissue diseases. Marine biotechnology constitutes a major component of the company's research efforts and remains a focal point of our drug discovery efforts. A very major component of our developmental plan is a joint academic-industry partnership supported by matching OsteoArthritis Sciences, Inc. funds and grant from the National Sea Grant Program to our university collaborators.

In this program, we have demonstrated that marine organisms are a rich resource of breakthrough drugs that will meet our therapeutic objectives. Working with Drs. Fenical, Faulkner and Jacobs of the University of California Sea Grant Program, we have identified several potent anti-inflammatory agents, such as pseudopterosins, which we will be evaluating in a variety of inflammatory diseases and developing for commercialization.

Other substances developed in this program are also scheduled for comprehensive pre-clinical development in the near future. Clearly, the therapeutic value of pseudopterosins would be unrealized without the close academia/industry collaboration established through Sea Grant efforts.

There is no question that our partnership effort with the Sea Grant scientists has been a major component of our success to date. However, if we are to continue this successful search for new marine-derived drugs, we need to ensure that federal funding of marine biotechnology within the National Sea Grant College Program network is adequate and to recognize the fact that this emerging leading edge technology is vulnerable to foreign competition. Research and development in biotechnology in the U.S. is facing increasing competition from abroad and this can result in an erosion of our competitive position in marine biotechnology.

How would additional support from Sea Grant have made development of your products easier or quicker?

7. Small companies can readily utilize the technology transferred from Universities. Additional support particularly supporting the efforts of chemistry and pharmacology will broaden the discovery potential for new products and speed up mechanism based investigations to bring forth the most unique natural product. Finding new resources during the study of marine natural products also assures us the opportunity of developing new drugs for the future. This is not possible without the special support provided by Sea Grant.

At what stage of developing a marine product is government support most critical?

8. Government support is essential during the discovery - screening stage (stage I), the mechanism based stage (stage II) and during preclinical development stage (stage III). These are the times of highest risk when success is most difficult. Clinical development and marketing should be supported by the private sector.

Besides research, how else could Sea Grant assist in getting marine products to market?

9. Sea Grant can assist by increasing support to University based chemists and pharmacologists. There may also be a special opportunity for Sea Grant to support later stage II work if there is a special initiative to support the preclinical development work that is necessary to evaluate a marine compound in the clinic. I strongly recommend that Sea Grant provides funding through a Small Business Industrial and Research (SBIR) system for small innovative companies to reach their Commercial objectives.

TESTIMONY

**United States House of Representatives
Committee on Merchant Marine and Fisheries
Subcommittee on Oceanography, Gulf of Mexico,
and the Outer Continental Shelf**

by

John E. Burris, Ph.D.

Director and Chief Executive Officer

Marine Biological Laboratory

Woods Hole, MA 02543

THURSDAY, APRIL 29, 1993

Thank you, Mr. Chairman and members of the subcommittee, for the opportunity to testify today on the importance of marine biotechnology and the need for a stronger Federal role in this area. My name is John Burris, and I am Director and Chief Executive Officer of the Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts. The MBL is the oldest marine biological laboratory in the United States, and we are among the leading institutions in the field of marine biotechnology in the world today.

Marine biotechnology represents an extraordinary opportunity to achieve a wide range of objectives that includes:

- o creation of new, high-tech jobs for the 21st Century;

- o promotion of economic growth and stimulation of new business opportunities;

- o development of new environmental and biomedical technologies;

- o improvement of America's global economic competitiveness in an emerging growth industry in which the United States currently leads.

Marine biotechnology offers a broad range of applications that will revolutionize our ability to better use marine resources and lead to the above objectives. I would like to highlight a few of these promising applications:

Pharmaceuticals and diagnostics: Considerable effort is being directed to searching for pharmaceuticals from the marine environment.

Encouraging results in this area include an analgesic and anti-inflammatory agent, manoalide, isolated from a marine sponge, an anticancer drug from a sea squirt, didemnin B, that is now in clinical trials, and a new class of antibiotics, the aplasmomycins, that are active against bacteria and the causative agent of malaria. Diagnostics continue to be sought, with one of the most successful marine biotechnological products being the extract from the blood of the horseshoe crab (*Limulus*) that is used as a test for endotoxin.

Biomaterials: In addition to pharmaceuticals, a wide variety of compounds are being sought from the sea. The best known of these are biopolymers such as agar and carrageenan that are extracted by traditional methods from marine algae. These biopolymers indicate the opportunities for other algal compounds to be extracted or for genetic manipulation of algae to produce more or different biomaterials. Another polymer, this

time from the foot of the common blue mussel, is an adhesive protein that may be used to repair knee ligaments or in dental cavities and skin grafts. There are also many enzymes found in marine organisms that will have applications. Already the high temperature stable enzymes isolated from bacteria found in deep sea vents have been commercialized for use in laboratories. These enzymes potentially could be important in other high temperature applications, such as laundry detergents.

Aquaculture and Seafood Safety: With a 1989 trade deficit of \$4.9 billion in fisheries products in the United States, it is clear that a market exists for seafood products that our producers are unable to meet. Enhancement of marine aquaculture using biotechnology is one way to help meet some of that demand. For example, the use of growth hormone with freshwater fish has led to remarkable increases in their growth rates. The breeding of a triploid strain of oysters now allows year-round oyster production, rather than just seasonal production. As Americans continue to eat progressively more seafood each year (one estimate by the Department of Commerce projects that U.S. seafood consumption could grow 30% by the year 2000), the safety of that seafood will be of paramount concern to the public. Marine biotechnology also offers sophisticated tests that will enable assays for ciguatoxin, a poison, in fish and *Vibrio cholerae*, the causative agent of cholera, in oysters. Others are in development to enable us to test for contaminated products and to learn more about the levels of toxins and how they enter the organisms.

Bioremediation: Improved methods to clean-up the marine environment following oil spills and the discharge of industrial and domestic wastes is another important application of marine biotechnology. The systematic screening of naturally occurring microorganisms or the enhancement of desired traits through genetic manipulation of the

microorganisms hold great promise for environmental clean-up by the organisms, rather than through chemical means. Most prominently featured has been the effort to develop "super bugs" that attack and breakdown oil, but bacteria are also able to remove toxic metals and metabolize other industrial wastes.

Understanding of the Oceans: The products of biotechnology have significant commercial applications. They will also be important as scientific tools that will enable us to learn more about marine life and the ocean environment. Genetic probes that allow us to track specific populations of organisms, such as salmon stocks, can tell us a great deal about the movement of the organisms and the waters in which they are found. We will be able, through increased understanding of the biology of microorganisms, to learn more about the cycling and consumption of many important elements and compounds including carbon dioxide, nitrogen, and phosphorus.

Marine biotechnology, as I have indicated, has shown significant accomplishments and will continue to offer great opportunities. It is a field, though, that is woefully underfunded.

For example, biotechnology is by far the largest interagency initiative in the Federal Coordinating Council for Science, Engineering and Technology (FCCSET) process, at more than \$4 billion in the President's budget request for FY 1994. However, marine biotechnology is a neglected stepchild in this process. Only about 1 percent of this initiative is for marine biotechnology research at universities and public research centers, where the greatest advances are being made. Total funding for marine biotechnology, including state, federal, and private industry, has been virtually flat since 1988.

The lack of attention in the U.S. also stands in sharp contrast to the high level of interest being shown in other countries. Japan in particular has embarked on a forward-looking investment strategy in which industry and government have agreed to provide nearly \$200 million for marine biotechnology in a decade-long program under the auspices of the Ministry of International Trade and Industry (MITI). We are seeing similarly strong commitments throughout the Pacific Rim, many of which are based on technologies pioneered in the U.S.

While the U.S. is currently the world leader in marine biotechnology, we will not retain this lead for long if we fail to respond to the competitive challenge we face. The U.S. simply cannot expect to survive in the global economy if we consistently allow foreign competitors to capitalize on technologies that the U.S. taxpayer has funded. It is essential to promote mechanisms for technology transfer together with partnerships between industry, academia, and the government to enable U.S. firms to bring products to the marketplace that are made possible through marine biotechnology.

I believe that the Marine Biotechnology Investment Act fulfills this objective, and more. It establishes a broad-based program within Sea Grant, together with a process to ensure that proposals are funded on the basis of scientific merit. It builds upon Sea Grant's record of leadership in marine biotechnology. It fosters the public-private partnerships that are needed to produce the products that will create jobs and economic growth. And it supports the training and education that will be needed to ensure that we have the human resources that are required.

Most importantly, it authorizes a significant increase in funding for marine biotechnology which, although tiny by comparison with the foreign

investment in this area, nonetheless represents a very substantial improvement in the U.S. commitment to this exciting field.

Mr. Chairman, I want to commend you for holding this hearing, and for playing a leadership role in bringing much-needed attention to the enormous potential of marine biotechnology. And I want to express my appreciation to Chairman Studds for introducing this important legislation. I urge the quick passage of the Marine Biotechnology Investment Act.

Again, thank you for inviting me to testify today, and I would be pleased to respond to any questions that you or other members of the subcommittee may have.



JOHN E. BURRIS
DIRECTOR
AND
CHIEF EXECUTIVE OFFICER

MARINE BIOLOGICAL LABORATORY

WOODS HOLE • MASSACHUSETTS • 02543 • (508) 548-3705

June 7, 1993

Congressman Solomon Ortiz
U.S. House of Representatives
Chairman Subcommittee on Oceanography, Gulf of Mexico, and
the Outer Continental Shelf
Room 1334, Longworth House Office Bldg.
Washington, DC 20515-6230

Dear Congressman Ortiz:

Listed below are my responses to the written questions sent to me following the April 29, 1993 hearing on the Marine Biotechnology Investment Act of 1993. I appreciated the opportunity to participate in the hearing and hope my responses are of assistance to you.

Question 1: We have heard many statements of the opportunities offered by marine biotechnology, as well as the federal government's commitment to the biotechnology field in general. What do you think is the reason for the federal government's ignoring of marine biotechnology?

Answer: The federal government has strongly supported biotechnology, primarily through its support of the basic research that provides the underpinning for biotechnology. Most of this support has come from the National Institutes of Health. The NIH has traditionally primarily supported research using terrestrial organisms. With only limited funds from the NIH, marine biotechnology research has had to rely on other agencies that have not had the resources to commit.

Question 2: You discussed in your testimony, the strength of the Japanese commitment to marine biotechnology. How are the Japanese approaching this area? Through academic investment? Federal laboratories? Are they targeting specific areas of potential?

Answer: The Japanese are investing in biotechnology through numerous avenues. There is a large commitment by industry to supporting this area. The Ministry of International Trade and Industry (MITI) along with 24 companies has established the Marine Biotechnology Institute (MBI) at a cost of approximately \$44 million. This institute has an operating budget of over \$20 million per year. Several of the Japanese universities are also doing basic research that might have applications for marine biotechnology. One estimate places Japanese investment in marine biotechnology at between \$900 million and \$1 billion per year.

Question 3: Is increased federal investment needed to maintain U.S. competitiveness in marine biotechnology? Are the amounts authorized in the legislation sufficient?

Answer: Increased federal investment is clearly needed to maintain U.S. competitiveness. The \$20 million proposed in the legislation will provide strong and necessary support for the U.S. to maintain competitiveness.

Question 4: In what specific areas of research, development, technology transfer, and education is this investment most needed?

Answer: The investment is needed in all areas - research, development, technology transfer, and education. No one area can be singled out as they are all interrelated. Allowing a group of independent, peer reviewers to decide on the proposals to be funded should insure that a proper mix is achieved.

Question 5: How can partnerships in marine biotechnology among government, industry and academia be best promoted?

Answer: Partnerships will be promoted when all of the participants feel that they are benefiting from the interactions. This means that funds are available to do the research and the outcome of the research is of interest or value to the other participants. There are no set formulas that apply; mutual benefit for all parties is the best guarantor of success.

Question 6: What insights can biotechnology provide into ecological and evolutionary problems and how can these lead to better resource management?

Answer: The potential applications of the techniques of molecular biology are numerous. Already molecular probes are being used to track populations of organisms in the terrestrial and the marine system. Using these probes one can follow specific populations of organisms and learn a great deal about their movement, as well as their patterns of reproduction. By learning more about organisms employing techniques of molecular biology we will be better able to culture these organisms, an extremely difficult task for many marine species. Molecular techniques are being used to study symbiosis - allowing us to learn more about this important relationship between species.

Question 7: What are the dangers of biotechnology development for the marine environment? What steps could or should be taken to address these?

Answer: Care should be exercised in the release of any genetically modified organisms. As the National Academy of Sciences has concluded: "Assessment of the risks of introducing recombinant - DNA - engineered organisms into

- 3 -

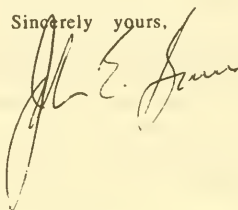
the environment should be based on the nature of the organisms and the environment into which it will be introduced, not on the method by which it was modified." Thus, the same level of care should be exercised in the release of organisms developed using the techniques of biotechnology that we already use in controlling organisms developed through more traditional genetic breeding techniques.

Question 8: What promise does marine biotechnology hold for enhancing the following areas of research and industry: aquaculture; bioremediation; seafood product safety; pharmaceuticals; polymers and lubricants?

Answer: My testimony already contains many of the promises of marine biotechnology. Further examples are available in the enclosed brochure entitled "Marine Biotechnology: Competing in the 21st Century" (a Sea Grant publication).

Again, thank you for inviting me to testify,

Sincerely yours,

A handwritten signature in dark ink, appearing to read "J. E. Smith". The signature is fluid and cursive, with the first letters of the first and last names being capitalized and prominent.

JEB:dmc

TESTIMONY

United States House of Representatives
Committee on Merchant Marine and Fisheries
Subcommittee on Oceanography, Gulf of Mexico,
and the Outer Continental Shelf

by

Dr. Rita R. Colwell

President

Maryland Biotechnology Institute

University of Maryland System

4321 Hartwick Road

College Park, MD 20740

April 29, 1993

Good morning, Mr. Chairman and members of the Subcommittee. I am Rita Colwell, founder and President of the Maryland Biotechnology Institute of the University of Maryland System. The MBI comprises four centers that conduct research and training in biotechnology, one of which is the Center of Marine Biotechnology, established in Baltimore in 1985. COMB is an emerging center of marine biotechnology that combines traditional marine sciences with molecular biology and molecular genetics.

I am here to add my voice to the views just expressed by Representative Hoyer and Dr. Burris on the unquestionable need for stronger Federal leadership and funding in the area of marine biotechnology research and development.

I have devoted much of my career to understanding marine microorganisms, and I cannot overemphasize the importance of marine biotechnology. This is one of the most exciting areas of the new scientific frontier, if only for the sheer raw potential of the great diversity of marine organisms that lie within the world's vast oceans. Marine biotechnology has made some extraordinary advances to date, despite scarce funding, and is already being applied to increase seafood production, develop novel pharmaceuticals, engineer

microorganisms that remove environmental pollutants, and develop new industrial materials. Researchers are also looking to the oceans as a source of clean energy and other products. These advances give a slight indication of the vast promise and enormous range of applications this field has to offer if proper commitment and funding are in place to support it.

Biotechnology is to society as the invention of the steam engine, the computer, and the splitting of the atom. The status of marine biotechnology today is analogous to that of the semiconductor industry in the 1960s: We are on the brink of a scientific revolution with monumental implications for the world's financial markets. The potential of marine biotechnology and its powerful new products to improve our lives and to increase our scientific understanding of the world around us is matched only by its potential for economic benefit. The question is whether it will be us or our international competitors that ultimately profit from this promising new technology.

To assess more accurately the prospects for marine biotechnology, the MBI, supported by Sea Grant funds, recently established a database to assess the status of marine biotechnology research and related industries in the U.S., Japan, and other industrialized countries. The preliminary findings of my colleagues and I were published earlier this month; I have included a copy of our results with my written testimony and ask that both be submitted for the record.

We found that in the U.S., marine biotechnology is very much in the formative stage, and that advances in the basic biological sciences are driving the development of the field. Despite the field's relatively small size and minuscule funding level, marine biotechnology has been surprisingly productive. In fact, we estimate that one patent has been approved for every \$1.1 million spent at universities and public research centers. We found that about 80 U.S. companies were dedicated to marine biotechnology or were sponsoring marine biotechnology research and development, most of which is devoted to natural products development, with promising results. Our data also

indicate that the significant advances made so far in aquaculture have not been demand-driven, as many believe, but rather resulted from technological advancements, most notably in genetic selection.

Overall, we found that U.S. industry has played only a minor role in marine biotechnology to date due to three main reasons: First, marine biotechnology and its promises are unknown to many firms and may be perceived as overly risky when offered the opportunity to enter the field. Second, most applications of marine biotechnology will be generated in the medium- to longer-term. U.S. companies -- particularly smaller start-ups that are underfunded themselves -- tend to plan for three- to five-year cycles, which excludes many research directions, including marine biotechnology, which is a relative newcomer. Third, unresolved issues with regard to field testing and release of genetically engineered organisms into the marine environment engender uncertainties among companies considering entering the field of marine biotechnology.

The ocean industry contributes more than \$100 billion annually to the U.S. economy, with nearly \$25 billion and one million jobs coming from fisheries alone. Despite these figures and the clear promise of marine biotechnology, total federal funding for marine biotechnology for FY 92 was only \$43.9 million. Funding for FY 93 increased by about \$6 million for applying molecular biological techniques to define oceanic processes. Total federal funding for all of biotechnology in 1992 was \$3.7 billion. Thus, only 1.2% of the federal biotechnology funding budget was devoted to marine biotechnology in 1992. For 1993, it remains the same. Without greater investment, it is doubtful that the U.S. will be able to maintain its present leadership position in this field.

U.S. researchers and federal funding agencies were the first to recognize the importance and promise of marine biotechnology, resulting in an initial spurt of growth in research and development in this country. In fact, I founded the Center of Marine Biotechnology in Baltimore in 1985 on funding provided by the Office of Naval Research,

under the University Research Initiatives. Unfortunately, funding levels have remained absolutely flat for the past three years, and no real growth for marine biotechnology can be expected during the next three years.

Significantly increased funding and a coordination of federal, academic, and industry efforts are absolutely critical for this field to experience the explosive growth that has occurred in biotechnology in general. This growth would be possible if industry were to become more involved in marine biotechnology -- an unlikely prospect for the foreseeable future, for reasons already mentioned. Unless a concerted national effort designed to yield marine biotechnology knowledge and processes is launched among the federal government, academe, and industry, the U.S. will forfeit leadership in this field to countries such as Japan, China, Taiwan, and Thailand, and U.S. advances will be limited to occasional chance discoveries of a process, activity, or application. As you have learned from other witnesses today, Japan, in particular, through a consortia of academic, government, and industrial organizations, has already seized upon marine biotechnology as an area worthy of national attention and development. In fact, at the Center of Marine Biotechnology in Baltimore, we have hosted dozens of delegations from Japan comprising scientists who wished to study COMB before setting up their own centers. Backing up this intensive national interest is a considerable financial investment in what they clearly believe to be a promising technology of the future.

Mr. Chairman, I believe that the bill before this committee is exactly what is required to ensure that the U.S. stays at the forefront of this promising frontier and does not relinquish yet another important new technology to overseas competitors. Equally significant, it places the right emphasis on the kind of high-technology partnerships among academe, government, and industry that this Administration wishes to promote.

I have long been on record that one of the best things our government has done is to establish the National Sea Grant College

Program. It is a genuine tragedy for this nation that the budget of Sea Grant, which provides an extraordinary economic return on investment (nearly 20 times the amount of the Federal contribution, according to one recent analysis), has declined in real terms by more than 50 percent since 1979. Sea Grant has been at the vanguard of marine biotechnology for more than a decade. I'm pleased to be able to share a very recent example of the results of Sea Grant's expertise and leadership in this area: When I leave here this afternoon, I will be heading for the Center of Marine Biotechnology in Baltimore to announce that one of our researchers has been successful in culturing in the laboratory one of the two disease agents that has devastated oyster populations and the oyster industry of the Chesapeake Bay in recent years. The breakthrough comes at the end of the worst oyster harvest in Maryland history, caused in large part by increasing levels of the deadly pathogen. Last Sunday, the Baltimore Sun ran an editorial about the plight of the oyster, essentially recommending resignation to the vagaries of nature and the ravages of these diseases on Maryland's signature water industry. With this new knowledge, provided by marine biotechnology, researchers will now be able to begin to develop gene probes to diagnose the pathogen in infected oysters and in bay waters and, eventually, to genetically engineer drugs that will stop the effects of this organism without harming oyster populations. The finding could have enormous implications for the oyster industry as well as the health of the Chesapeake Bay. The breakthrough was made possible through Sea Grant funding.

Sea Grant has done more than any program I know of to inform businesses of advancement in basic marine biotechnology research and to help them apply those advancements, resulting in new products, new companies, new jobs, and economic stimulation that is so desperately needed in our economy. Sea Grant's combination of top-quality research, education, and outreach through its marine advisory services is particularly well-suited to spur advances in research, application, and public awareness in marine biotechnology. It is entirely appropriate, therefore, that the Marine Biotechnology Investment Act of 1993 implement this new initiative through the National Sea Grant

College Program.

I also wish to register strong support for the way by which these new funds will be administered: the bill establishes a national review process that will award grants based on merit and ensures that projects will be evaluated competitively, and on a level playing field. This is the best way to ensure that only proposals of the highest quality and promise are funded.

To summarize, marine biotechnology represents one of the greatest frontiers of intellectual and commercial endeavors in the marine sciences for the remainder of this century and for decades in the 21st century. If we are to realize its benefits, we must organize concerted support of this emerging technology. Sea Grant is clearly the appropriate federal program to direct funding for marine biotechnology, with proven capability in identifying and funding promising research, training researchers for a work force that will be needed in marine biotechnology, advancing public awareness and education in biotechnology, and promoting cooperation among industry, academe and government. There is a growing cadre of exceptionally capable researchers with the knowledge of both the new sciences -- especially molecular biology -- and the traditional marine sciences, ready to make the advances that this bill envisions. Sea Grant, one of the most competitive sources of marine science support, is perfectly suited to administer an increase of funding. It has the infrastructure to support deserving proposals that until now have had to be declined because of the lack of resources, with minimal increase in administrative overhead. All of these considerations are essential to fulfilling the objectives of this bill and ensuring that the funds authorized are spent wisely.

I cannot overemphasize the importance of increasing federal spending on research and training in the application of molecular biology to ocean sciences. I urge you to support this bill, and I would be pleased to respond to any questions you may have.

GENETIC ENGINEERING NEWS

APRIL 1, 1993

BIOTECHNOLOGY • BIOREGULATION

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Survey Indicates Marine Biotech Industrialization Moving Is Slowly

By Rita R. Colwell, D.Sc., Ph.D.,
and Raymond A. Ziilskas, Ph.D.

The Maryland Biotechnology Institute (MBI, College Park), supported by Sea Grant funds, has undertaken an assessment of the status of marine biotechnology research and related industry in the U.S., Japan and other industrialized countries. For this study, we developed a database dedicated to marine biotechnology called MARBIO. To collect data for MARBIO, detailed questionnaires were sent to a representative sample of U.S. scientists in research institutions and private companies. Some of the preliminary findings are summarized below.

As is required in any such study, it was necessary to define "marine biotechnology." After having asked approximately 40 scientists how they defined the term, we settled on a definition closely resembling one adopted in 1981 by the Organization for Economic Cooperation and Development (OECD) for "biotechnology," namely, marine biotechnology is "the application of scientific and engineering principles to the processing of materials by marine biological agents to provide goods and service." Marine biotechnology holds particular promise for industry in applications in seven sub-areas: aquaculture, marine natural products, bioremediation, biofilm/bioadhesion, cell culture, biosensors and terrestrial agriculture.

U.S. Research

An analysis of the MARBIO data gathered to date revealed that in 1991, about \$44 million was spent on research at universities and public research centers for marine biotechnology. The major federal funding sources were the NIH (28%), NSF (13.5%), ONR (Office of Naval Research) (9.4%) and Sea Grant (8.8%). In addition, state funding provided about 7%, while private industry funded less than 7% of the



Depiction of the interrelationship between the ocean sciences and biotechnology that describes marine biotechnology.

research performed at these laboratories. Although funding for marine biotechnology research grew rapidly with the emergence of this technology, our respondents reported that funding was flat during 1988-1991.

State Centers

Between 1988 and 1991, three states, Maryland, North Carolina and California, established dedicated marine biotechnology centers. While the centers in California and North Carolina were built with funds provided by the respective states, major funding for the Maryland center was provided by ONR under the University Research Initiatives. This program is presently funding establishment of two additional research centers, in California and Tennessee, that will be dedicated largely to marine biotechnology.

Analysis of MARBIO data shows that the major marine biotechnology research areas are basic research in microbiology and molecular biology (34%), followed by research related to pharmaceuticals or fine chemicals (14.6%), environment and/or bioremediation (12.6%) and aqua-

culture (11.7%). Clearly, in the U.S., the basic biological sciences are driving the marine biotechnology engine—further evidence that this field is very much in the formative stage.

\$1.1 Million=1 Patent

Despite its small size and low funding level, marine biotechnology has, to date, been productive. From the MARBIO data we estimate that for every \$1.1 million spent in research at university and public research centers, one patent has been approved. Since a trend seems to be developing where researchers change from their current focus on basic research to research that has more possibilities for commercial application, this patent activity has already increased.

Issues related to biosafety have, to date, not been a barrier to the advancement of marine biotechnology. Approaches that have been developed to ensure safety in general biotechnology research and testing activities apply directly to marine biotechnology. But, as was indicated by the concerns demonstrated by environmental groups in 1990, prior to the testing of transgenic carp in closed facilities in Alabama, open field testing of transgenic marine organisms may generate public controversy. Therefore, it is not too soon to assess possible risks associated with conducting open, large-scale field trials of transgenic fish, marine plants and marine bacteria. Until this public biosafety issue is resolved, industrial interest in this aspect of marine biotechnology will lag.

U.S. Companies

Our survey of U.S. companies found that about 80 were dedicated to marine biotechnology or were sponsoring marine biotechnology R&D, either in-house or extramurally. Survey questionnaires sent to research directors of these companies yielded a useful set of data recorded in MARBIO. Most of the ef-

fort by industry is devoted to natural products development. Approximately three pharmacological agents that show activity against tumors and viruses or are active against psoriasis are in clinical trials. Another five compounds have shown promise in these areas and are in preclinical trials.

Many believe that advances in aquaculture have been demand driven. Our data indicate a different conclusion—it is technological advancement, notably genetic selection, that has allowed this industry to take off with a few successful products such as catfish. The tools of marine biotechnology will be necessary for development of future innovations in aquaculture and to allow closed system production to become economically feasible in the U.S.

The area of marine biotechnology that will have the most significant economic impact in the short term is marine bioremediation. However, even this industry will, for the foreseeable future, have to rely on naturally-occurring marine microorganisms, some of which will be developed for greater efficiency via classical techniques of breeding and selection.

The U.S. Industry

The U.S. industry has played a minor role in marine biotechnology to date. We postulate that there may be three main reasons for this seeming indifference to the field. First, marine biotechnology is unknown to many firms, therefore they believe it to be overly risky when offered the opportunity to enter the field. Ocean resources have a history of being difficult to find and reach, and even after being located, strenuous efforts are required for exploitation on a dependable and sustainable basis. Companies do not realize that further work in the field may remove this impediment.

Second, most applications from the seven sub-areas of marine bio-

technology that we are examining in our study will be generated in the medium-to-longer term. U.S. companies, especially smaller biotechnologies, tend to plan for three-to-five-year cycles, which exclude many research directions, not only marine biotechnology.

Third, while the biosafety issue has not significantly affected the advancement of marine biotechnology to date, uncertainties may affect future development and therefore must be addressed. Until these uncertainties are cleared up, some companies will continue to hesitate in making long-term commitments to marine biotechnology product development in regard to transgenic organisms.

Researchers and funding agencies in the U.S. were the first to recognize the importance of marine biotechnology, resulting in an initial spurt of growth in R&D in this country. However, funding levels have remained flat for the last three years and, unfortunately, no real growth for marine biotechnology can be expected during the next three years. Unless funding for marine biotechnology increases significantly, the explosive growth that has occurred in biotechnology in general cannot happen for marine biotechnology. However, growth is possible if industry was to become more interested in marine biotechnology, an unlikely prospect since so few applications from this field are in the pipeline. Unless a major concerted effort is launched, advances in the U.S. will be limited to occasional chance discoveries of a process, activity or application. A national effort designed to yield marine biotechnology products and processes could be successful, and would yield a far greater return than merely relying on chance.

Potential of the Field

It is useful to note that marine biotechnology has enormous potential for developing countries where seafood is a major staple. In Ecuador, for example, shrimp culture provides a major export product, perhaps 40% of the gross national product. Similarly, Taiwan's aquaculture industry is major in its scope and tonnage. Investment is beginning to be made in marine biotechnology in these countries because of the advantages offered in improvement of other aquaculture activities, as well as natural products exploitation. It should also be noted that because only the genetic material need be "harvested," depletion of the resource in nature is avoided, a major benefit of utilizing biotechnology.

Selected Companies Involved in Marine Biotechnology*

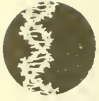
Schering-Plough Corp. Madison, NJ	Screening for marine natural products.
SmithKline Beecham King of Prussia, PA	Enzyme inhibitors, receptor antagonists with potential medicinal applications.
Cyanotech Corp. Kailua-Kona, HI	Natural products from micro-algae.
Martek Corp. Columbia, MD	• • •
Microbio Resources San Diego, CA	• • •
FMC Corp. Rockland, ME	Macroalgae, carrageenans and seaweed hydrocolloids.
New England Biolabs Beverly, MA	Thermostable enzymes from marine organisms.
Solis Nova Baltimore, MD	• • •
CytoCulture Int'l., Inc. Point Richmond, CA	Biotech wastewater as carbon source for aquaculture.
Mariculture Inc. Wrightsville Beach, NC	High-value fine chemicals and pharmaceuticals; cell culture systems; unusual lipids, carotenoids, xanthophylls and retinoids.
Human Technology Corp. Anvada, CO	Production of biomass and extraction of natural products and fine chemicals.
W.R. Grace & Co. Columbia, MD	Enzyme production by marine microorganisms for health care.
CalBioMarine Technologies Inc. Laurel, CA	Whole-animal marine invertebrate ecoculture for biomass production to yield secondary metabolites; invertebrate cell culture system for novel chemical agents.
American Cyanamid, Lederle Labs Pearl River, NY	Natural products; marine macro- and micro-symbionts.
Zoming Corp. Midland, MI	Anti-fouling.
Marine Environmental Research, Inc. Moonhead City, NC	• • •
Princeton Polymer Labs Plainsboro, NJ	Polymers and polymer related macro- and micro-symbionts. Products of microalgae.

*Data from MARBIO database located at University of Maryland, College Park.

The benefits of marine biotechnology can be readily enunciated, but unless the decision to invest appropriately in this young technology is made, the "winners" will not be in the U.S.

A report on the results of the MARBIO study will be published shortly. Once the report is published, the MARBIO database will be accessible to any researcher.

Rita R. Colwell, D.Sc., Ph.D., is president of the Maryland Biotechnology Institute in College Park and professor of microbiology at the University of Maryland. Raymond A. Zilinskas, Ph.D., is an associate professor at the Maryland Biotechnology Institute.



June 2, 1993

Maryland
Biotechnology
Institute

Representative Solomon Ortiz
Room 1334
Longworth House Building
Washington, D.C. 20515

Dear Representative Ortiz:

As a follow up of my testimony on April 29, 1993 before the United States House of Representatives, Committee on Merchant Marine and Fisheries, Subcommittee on Oceanography, Gulf of Mexico and the Outer Continental Shelf, following are my responses to your questions.

If you have any further questions, please do not hesitate to contact me.

Best wishes,

Yours sincerely,

Rita R. Colwell, Ph.D., D.Sc.
President
Maryland Biotechnology Institute
and Professor of Microbiology

RRC/mj0603

OFFICE OF
THE PRESIDENT
1123 MICROBIOLOGY
BUILDING
COLLEGE PARK, MD 20742
(301) 405-5189
TELEX 5106010426
FAX (301) 454-8123

Answers to Questions of Dr. Colwell
from Representative Solomon Ortiz

1. Of the 80 companies engaged in marine biotechnology that we surveyed in 1991-1992, 19 (44%) were subsidiaries of very large corporations, such as Abbott or Monsanto, and the remainder (61 or 56%) ranged in size from medium 100-500 employees) to very small (4 employees).
2. The question of how much U.S. industry is investing in marine biotechnology is difficult to estimate since some companies doing R&D related to natural products do not distinguish between organisms collected from the terrestrial and marine environments. However, based on our survey of companies conducted in 1991-1992, we estimate that the investment at that time by industry in marine biotechnology was \$7 - 15 million per year. Keeping in mind that the same uncertainties are present in regards to Japanese industry, we estimate that it invests approximately \$800 million per year in marine biotechnology. The enormous difference stems from two reasons: First, the total investment in Japan is much greater (about \$1 billion per year versus about \$50 million in the U.S.) and, second, that the major funder of marine biotechnology R&D in the U.S. is the federal government, while in Japan, it is industry.
3. Yes, these are tight budgetary times that are particularly stressful to states with large deficits. The Sea Grant Program, by statute, is required to seek match from grant recipients. In the past, this has been problematic, particularly for private institutions without resources to contribute. Most state institutions have been able to provide the necessary one-third match fairly easily. Given the enormous pressure on state budgets, one can expect even these institutions to have potential problems in the future. This will vary on a state-by-state or case-by-case basis. Congress may wish to exempt the biotechnology funding from the match requirement, or indeed, reconsider the match requirements for Sea Grant during the next reauthorization in 1995.
4. Both federal laboratories and academia have the capabilities to conduct marine biotechnology research. These capabilities vary from institution to institution. Many of us feel that the competitive process by which academic institutions submit proposals to peer review, as in the case of proposals to Sea Grant, offers the best prospects of leading to the strongest research with the best possibility of success. Federal laboratories will benefit if they, too, are constrained by the same rules of fair open competition of ideas with appropriate peer review. Thus, if federal laboratories are to engage in this research, it should not be done by simple line appropriate to such laboratories.

There is strong evidence that new models of federal/academic/industry partnerships will be especially important components of biotechnology research and technology transfer. One example of a partnership involving federal and academic laboratories is near and dear to my heart. The Center for Advanced Research in Biotechnology (CARB) is an example of a partnership between the National Institutes for Standard and Technology (NIST) and the Maryland Biotechnology Institute (MBI) of which I am President.

5. Although the last two administrations have asked for small or no budget requests in behalf of the National Sea Grant College Program, fortunately Congress has provided enough funding to keep the program fully functional. Sea Grant has, in place, the capability and infrastructure to manage easily a marine biotechnology program on the order of \$20 million. With the change in administrations, we sense that Sea Grant is again becoming a priority of the Executive Branch. Moreover, although NOAA has failed in the past to respond in any substantial way to the FCCSET Biotechnology cross-cut, we hear rumors that plans are being made to redress this oversight in next year's budget requests.

Sea Grant not only has the capability to sponsor research in biotechnology, but the record is clear that the Sea Grant network has provided considerable leadership in this area over the last decade. Indeed, I testified before your very committee, along with several other Sea Grant directors in 1985, about the need to establish a research program in Sea Grant in marine biotechnology. Please note that this occurred well before any federal effort was established in biotechnology. Even with its meager resources through the 1980's, Sea Grant continued to support research in marine biotechnology, although nowhere near the level that it could have. In my view, Sea Grant, with its unique mission to conduct research and provide for technology transfer, is particularly well positioned to serve as a focal point of federally sponsored marine biotechnology research.

6. Without any doubt, increased federal investment is needed to maintain U.S. competitiveness in marine biotechnology. This area is woefully underfunded at present, with respect to our major international competitors. Congress has the opportunity to redress this problem through this bill.
7. Basic and applied research is required in the following primary areas. Because of the relative infancy of marine biotechnology research, investment within these research areas is needed at all levels, that is in basic and applied research, technology transfer, and education.

1. Molecular genetics of marine organisms. A fundamental understanding of the molecular genetics of marine

animals, plants, and microorganisms forms the critical basis of biotechnology applications. Knowledge of the molecular biology of specific processes provides the potential for control of these processes, as well as the development of genetic diagnostic tools to monitor ecosystem processes.

2. Aquaculture. There is enormous potential for dramatic advances in aquaculture, to optimize production of organisms that are currently grown in aquaculture facilities and to extend the range of organisms and environments that are amenable to culture in contained systems. For example, considerable advances have been, and are being made in enhancement of growth, development, reproduction, and disease control and prevention of fish and shellfish. However, we have only begun to explore the potential of molecular techniques for improving the effectiveness and range of aquaculture marine and freshwater organisms.
3. Bioremediation. It is clear that current technology, which relies heavily on chemical treatment or physical containment is inadequate for dealing with existing and future pollution of marine, terrestrial, freshwater, and groundwater environments. Bioremediation, that is the utilization of in situ biodegradation by naturally occurring or introduced organisms, holds considerable promise for improving the efficiency of contaminant clean-up and providing cost-effective procedures. Marine microorganisms can be utilized or augmented to degrade pollutants, or novel marine organisms with novel degradative pathways for processing a variety of contaminants may be discovered in marine systems.
4. Biofilms and Biocorrosion. Biofouling and microbially induced corrosion of surfaces impose major costs to commercial and naval shipping. Many descriptive and experimental studies have been carried out on these processes, but there is a paucity of understanding of the molecular basis of these biological events. Knowledge of the genetics of biofouling and biocorrosion may allow the development of novel methods for their prevention or control.
5. Natural Products. There is enormous potential for identifying new biological compounds, such as pharmaceutical agents and enzymes, that will have a variety of commercial applications. Marine organisms have evolved in many cases chemical means of communication, and these bioactive compounds may have enormous potential for bioprocessing and medical applications.

8. Sea Grant is, by its very nature, a partnership activity between the federal government, academe and industry. The federal government, needs to nurture and develop Sea Grant to capitalize on this opportunity. First, NOAA must use Sea Grant more effectively as its conduit to the academic world. NOAA Sea Grant staffing should be developed to provide for better technology transfer between Sea Grant and its activities and Executive Branch agencies. Second, The Department of Commerce (DOC) must use NOAA to achieve its ends to promote economic development while still protecting the environment. This will require DOC to recognize and exploit the talents of NOAA and the Sea Grant network. Beyond this, as I have stated above, the federal government should continue to explore developing cooperative relationships between federal and academic laboratories in the CARB model.
9. Biotechnology offers many insights into ecological and evolutionary problems. Modern molecular tools are essential to the study of phylogeny. They also enable scientists to isolate, enumerate and identify organisms with key ecological functions. They help us understand, using molecular probes, the structure and function of marine microbial communities, for example. I call your attention to the brochure produced by the Sea Grant network, "Marine Biotechnology," which provides more information relevant to this question on pages 8-13 and 16-17.
10. The dangers of biotechnology development are in my opinion, overstated, especially as they pertain to a program that focusses on research in biotechnology as its first priority. Nonetheless, the public has a right to be concerned about misapplications of this and any technology, and we have an obligation as scientists, to respond to such concerns. It is unlikely, though conceivable, that some genetically engineered organisms could be released that could displace natural flora and fauna. Incidentally, I predict that the release of the Stephen Spielberg film Jurassic Park on June 11th will greatly spur public concern about such problems. Clearly, we are obliged to make and have developed sensible precautions to prevent irresponsible introductions of genetically altered organisms. When we established the Maryland Biotechnology Institute, we recognized that there are legitimate policy and ethical questions that relate to this technology, accordingly, we established the Center for Public Issues in Biotechnology. Centers such as this could benefit greatly from the availability of funding directed to support policy and ethical studies.
11. Marine biotechnology can be applied to enhance research and industry as follows:

Aquaculture. Marine biotechnology may be deployed to increase yields from aquaculture or to enhance the quality

of its products. In particular, biotechnology offers new methods to improve the health status of cultured organisms and to regulate growth and reproduction of commercially important finfish, crustaceans, bivalves and algae. Specifically, cultured organisms can be induced to:

- grow faster
- become more disease resistant than present species
- grow in colder, warmer, shallower or deeper water than is now possible
- possess better nutritional characteristics than present species
- produce new or unique products
- if alga, contain fewer impurities that complicate processing
- if alga, yield higher concentrations of desired products
- if alga, produce more biomass per cubic unit.

Bioremediation. The environmental remediation industry is experiencing tremendous growth in all industrialized countries. Increasingly, it applies bioremediation in many projects because this set of techniques has three major advantages over conventional techniques. First, the employment of bioremediation to process waste water is less costly, in terms of both capital expense and operating costs, than alternative techniques commonly used in primary and secondary waste water treatments. It is significantly less costly than incineration. In general, bioremediation requires rather low capital investment, has low energy consumption, and remains self-sustaining. Second, bioremediation is more environmentally benign than alternative waste water techniques or techniques used to treat polluted or degraded soil. Bioremediation is thus preferable to land-fills, surface impoundment, chemical treatment of toxic dumps, and incineration. Third, in some cases of marine pollution there is no real alternative to bioremediation, excepting natural processes, because conventional clean-up techniques, consisting of skimming oil from the water surface, mopping up oil by hand using paper towels, cleaning sand and stone with high-temperature pressurized water, and employing chemical dispersants and surfactants, would be too damaging to fragile ecosystems.

Seafood product safety. As is well known, seafoods are consumed throughout the world, providing high quality protein and other important dietary constituents. However, seafoods can be the source of foodborne diseases due to infectious organisms or toxins. Seafoods have been implicated as the vehicles for 10% of all foodborne diseases in the U.S., 7.6% in Canada, and 13.2% in the Netherlands. There is intense interest in industry to develop biosensor kits designed to detect increased levels of specific pathogens and toxins in seafood. Kits based on

monoclonal/polyclonal antibodies seem to hold particular promise in the short term. As kits are marketed and used routinely in the seafood industry, contaminated batches of seafood will be detected early and prevented from reaching consumers. A marked reduction in the incidence of foodborne diseases will undoubtedly follow, saving millions of dollars in health costs and preventing much misery.

Pharmaceuticals. Natural resource chemists have for over 100 years been screening the world's organisms for useful chemical substances. The results of this effort is impressive; about 20,000 chemicals from natural products have been characterized and the annual sales of pharmaceuticals derived from plants reaches \$10 billion per year in the U.S. alone. Yet little or nothing is known about the chemical composition of most existing terrestrial plants and microorganisms; those inhabiting the marine environment are even more alien. The marine environment therefore, is the largest untapped resource for organisms that contain or excrete compounds having potential as pharmaceuticals and specialty chemicals.

By and large, chemicals constituting organisms fall within one of two groups. First, there are primary and intermediate metabolites and cofactors, which are essential for the growth of the organisms and its reproductive metabolism. Second, there are secondary metabolites, i.e., substances that have no essential function and whose reason for existence are not so clear. Secondary metabolites have diverse chemical structures, but smaller groups of organisms, such as genus, species, or even strain, often produce substances distinct to that group. Secondary metabolites are by far the most important group of useful chemicals produced by marine organisms; their range of pharmacological properties encompass antibiotics, anti-inflammatory agents, anti-tumor and anti-viral agents, toxins, enzymes, and pesticides chemicals. As of this writing, more than 2,000 secondary metabolites showing bioactivity have been isolated from marine organisms. Development of about nine of these compounds have proceeded to the stage of clinical testing.

Polymers and lubricants. When a man-made object is submerged in ocean waters, marine bacteria quickly begin to settle on its surface. If the settlement process is allowed to proceed, the initial film consisting mostly of microorganisms soon attracts micro-algae and, eventually, animals such as barnacles and mussels. Surface colonization will damage the object via two types of actions. First, as an ever increasing number of organisms become enmeshed in the biofilm, a noticeable fouling of the surface will occur, leading to encrustation. If the surface in question belongs to a ship, biofouling will increase vessel drag, thereby, reducing its speed and increasing fuel consumption. It has

been estimated that a 200 micron thick encrustation on a ship's hull can decrease that ship's speed by 20%. Second, some of the organisms constituting the biofilm produce metabolic by-products which corrode metals. Sulfate-reducing bacteria, in particular, attack metal surfaces, causing local pitting that can lead to catastrophic failure of equipment. Bacterial corrosion is exceedingly damaging; a 1.75 cm thick steel plate may be penetrated in about six months. Piers, off-shore drilling structures, and Ocean Thermal Energy Conversion devices are especially prone to damage by organisms constituting the biofilm.

Marine biotechnology research is being directed at solving the problems related to biofilms and biofouling and, concurrently, at securing benefits from the natural biochemical processes underlying these phenomena. For example, some research aims to clarify the process of bacterial colonization, particularly identifying the genes that control attachment. Research results may be used to develop coatings that cannot be sensed by the colonizing bacteria. Without this stimulus, they are unable to settle. Yet other scientists are concentrating on the second step in biofouling -- when invertebrates respond to chemicals exuded by colonizing microorganisms by settling on top of them. It may be possible to interfere with the function of the invertebrates chemical receptors through the release of harmless substances, making it impossible for these organisms to identify favorable settling sites.

Research to solve the nettlesome problem of biofouling can, at the same time, be useful in developing products and processes. In fact, the first industrial chemical to result from marine biotechnology is a bioadhesive, i.e., a glue produced by mussels to anchor itself to hard surfaces. The advantage of this glue is that it sets strongly underwater, making it useful for dental and surgical procedures, as well as for certain scientific work. For example, the adhesive from the foot of the blue mussel has been isolated and its chemical structure is being unravelled. A synthetic gene that codes for a protein having a structure that is 40% similar to the mussel's glue has been constructed and introduced into the genome of an industrial yeast; then the engineered yeast was grown in fermenters where it produced comparatively speaking large quantities of the glue. A commercial product called AdheraCell was first marketed in April 1990 for use in cell and tissue culture.

Testimony of Samuel H. Wilson, M.D.
Director, Sealy Center for Molecular Science
Professor, Department of Human Biological Chemistry and Genetics

House of Representatives Committee on Marine and Fisheries
Subcommittee on Oceanography, Gulf of Mexico and
Outer Continental Shelf

Representing
The University of Texas Medical Branch at Galveston

Concerning Marine Biotechnology Program Act of 1993

Longworth House Office Building, Room 1334

10:00 A.M., Thursday

April 29, 1993

Thank you, Chairman Ortiz and members of the Subcommittee. I am Samuel H. Wilson, Director of the Sealy Center for Molecular Science at The University of Texas Medical Branch at Galveston. I have been a biomedical research scientist for over 25 years. I spent 24 years on the staff of the National Cancer Institute before moving to Galveston. I am here today to represent marine biotechnology researchers in the Texas-Gulf Coast Region.

Thank you for this opportunity to testify on the Marine Biotechnology Program Act of 1993. My testimony will focus in two areas. They are: 1) merits of marine biotechnology research in the Texas-Gulf Coast Region; 2) comments on the Bill itself. I would like to discuss biomedical applications of marine research at the molecular level.

1) As you have already heard, Mr. Chairman, marine biotechnology has a very wide range of applications. Through the phenomenal advances of molecular biology we are now in a unique position to take advantage of a new technology to enhance marine life. Thus, one of the most promising and wideranging techniques in this field lies in understanding, and intelligently altering, the genetic structure of organisms. This genetic research is generally considered to be one of the most advanced areas of biotechnology, and because of the wealth and diversity of marine organisms and the unique substances they contain, biotechnology at the molecular level is an area where revolutionary advances can be made. As has been true of revolutionary technologies of the past, we cannot even begin to foresee many of the applications that will become commonplace. However, significant advances have already been made through marine biotechnology at the molecular level, including aquaculture, genetic mapping and identification of fish stocks, prevention of disease in several commercially important species, and synthesis

of natural marine products. With the resources that are needed, much more can be done.

I speak on behalf of a large group of marine biotechnology researchers: Scientists at Texas A&M University are conducting genetic studies of marine animals (L. DiMichele, B. Neill, J. Gold); a scientist at the Port Aransas facility (P. Thomas) is collaborating with scientists at the University of Texas Medical Branch (B. Thompson) to genetically alter fish; scientists at Southwest Texas State University and at M.D. Anderson Cancer Center in Smithville (R. Walter, D. Morizot and R. Nairn) are cloning DNA repair genes of fish, and Dr. Morizot has been instrumental in constructing a genetic map of one species of fish. Such a genetic map is required for molecular experiments in fish genetics. Scientists at Texas A&M in Galveston are analyzing genetic damage after environmental exposure in fish and other marine organisms (Dr. Giam), and scientists at the Marine Biomedical Institute at the University of Texas Medical Branch in Galveston are conducting similar DNA analysis studies (J. Liehr, L. Lu and R. Hanlon). Scientists at the Institute of Biotechnology, Texas A&M University in Houston (C. Arntzen, R. Wells) are genetically altering marine plants, so as to immunize animals in aquaculture systems in order to control diseases. This last group has a close linkage and working relationship with the Sealy Center for Molecular Science at the University of Texas Medical Branch at Galveston. Collectively, we are in a position to take advantage of new molecular technologies, and to have a real impact on marine biomedical technology in the future.

I will now discuss biomedical applications of research in the field of marine biotechnology, particularly in the area of DNA repair/environmental science, which is a top priority for my institution.

Mr. Chairman, we live in a world that poses continual threats to our chromosomes and the genetic material therein, DNA. Ultraviolet light from the sun and a multitude of chemical agents can cause damage to our DNA, and this, in turn, can rapidly lead to cell malfunction and death. DNA damage usually does not cause cell death in normal healthy cells because DNA damage is rapidly corrected by a process called DNA repair. Therefore, the repair of DNA must be regarded as one of the essential events in all life forms, and there is much recent excitement in this field of research because of the increasing awareness of the relevance of DNA repair to human health. Damage to DNA has been clearly implicated in cancer, and there have been suggestions that it may be a component in the biology of aging as well. Many spontaneous abortions and some congenital defects may represent adverse consequences of unrepaired or misrepaired DNA damage in embryonic cells. The interest and concern of the general public has increased as the list of known carcinogens in our environment expands.

The main scientific themes of the Sealy Center are identification of new human DNA repair genes and structural studies of their protein products. Our ultimate goal is to manipulate DNA repair in the living cell with detailed knowledge of how the individual DNA repair proteins function. Such manipulation will allow us to increase the resistance of cells to environmental hazards and toxic agents. Drs. R. Walter, R. Nairn and D. Monizot have recently discovered that DNA repair genes in fish are very, very similar to those in humans. Fish are much easier to study genetically than higher organisms. Therefore, we have decided to collaborate with marine molecular biologists to genetically manipulate marine animals to study and improve DNA repair.

We believe that rational drug design to control the harmful effects of genotoxic agents

can be accomplished through a structural and mechanistic understanding of the function and regulation of key DNA repair proteins. We are developing a process that will eventually yield a precise understanding of the function of each protein. Our long-term goal is to determine whether drugs designed to enhance the function of the proteins can control or eliminate gene damage after exposure to toxic substances. Among the most promising applications include:

- repairing DNA damage caused by ultraviolet light. If we are successful in introducing a DNA repair substance as a new ingredient in sunblocking lotions, it might be possible to prevent many cases of skin cancer.
- reduce workplace hazards from exposure to toxic chemicals. One of the most common forms of DNA damage is alkylation, which is caused by industrial chemicals such as ethylene oxide and vinyl chloride, or by potent carcinogens called nitrosamines. When exposure is left untreated, these chemicals attach to the DNA, where they interfere with the cell's ability to transcribe and copy genetic material. This can lead to mutations that eventually cause cancer. The Sealy Center is actively pursuing drugs designed to halt this genetic damage, and thus prevent cancer. Genetic studies of fish will certainly speed progress in this area.

2) Concerning the Bill, we believe it is good that the Bill reserves money outside the college level, and it is good that the Bill puts review at the national level, as the local review process can not bring the appropriate expertise to the subject matter.

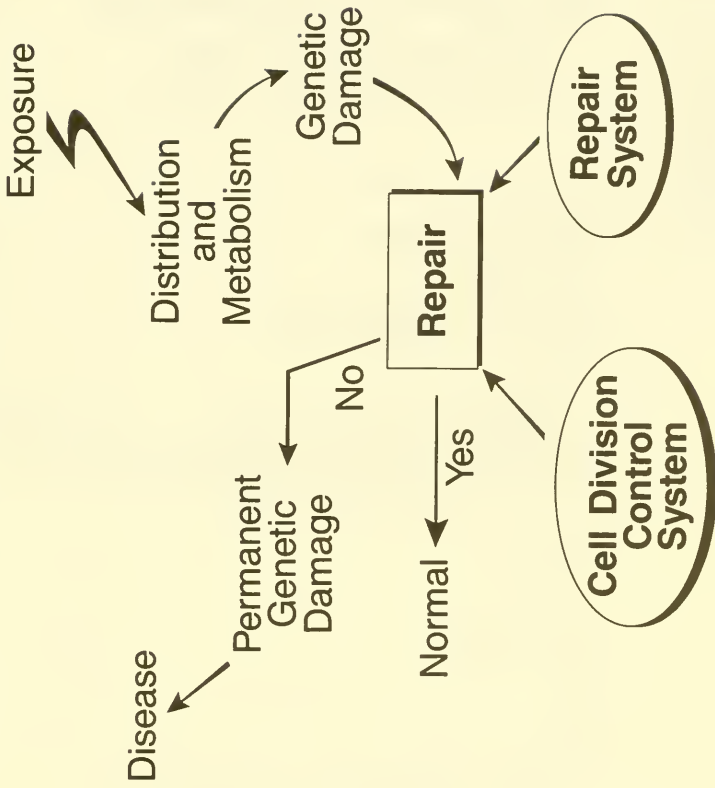
It should be clearly stated in the Bill that funding is for "Investigator-initiated applications." This will insure that the best scientific facility, chosen through the time-tested and effective peer-review process, is selected to conduct this research.

The emphasis should be at the basic science level, i.e., the discovery and isolation of molecular tools, and on development phases. Application trials, grow-outs, etc. should revert to other grant opportunities. Thus, the Bill should allow the development of molecular tools for ecological study as valid new products, but exclude the application of already mature molecular technologies (e.g., genetic stock assessments), since these have already been adapted for use by state and federal agencies. Wording is important here, because we don't want to exclude the development of new technologies for the same purpose.

We recommend considering longer grant cycles for this program. Sea Grant normally operates on two year cycles. This is not long enough for reasonable progress on molecular biotechnology startups. Three to five years would be better.

In closing, I repeat that through advances in molecular biology, we are now in a position to take advantage of a new technology to enhance our understanding of marine life and to enhance the way marine organisms respond to toxic materials. This research can also have an impact on treatment and control of cancer in humans.

OVERVIEW



The University of Texas Medical Branch at Galveston

Sealy Center for Molecular Science

**Administrative Staff**

Samuel H. Wilson
Director
Geraldine M. Wollie
Executive Director
Ernest Leal Jr.
Business Manager

Scientific Staff

Allan R. Brasier
Miriam Falzon
Julie K. Horton
Rolf König
Amalendra Kumar
R. Stephen Lloyd
Sankar Mitra
Javier Navarro
Louise Prakash
Satya Prakash
Melvyn Soloff
Steven G. Widen
Samuel H. Wilson
Thomas G. Wood

June 29, 1993

The Honorable Solomon P. Ortiz
Chairman
Subcommittee on Oceanography
Gulf of Mexico and the Outer
Continental Shelf
U.S. House of Representatives
Committee on Merchant Marine and Fisheries
Room 1334, Longworth House Office Building
Washington, D.C. 20515-6230

Dear Mr. Chairman:

As requested in your recent letter, it is my pleasure to provide you with the enclosed responses to the questions submitted for the record as follow-up to the hearing on the Marine Biotechnology Investment Act of 1993 held on April 29, 1993.

Please let me know if I can be of additional assistance.

Sincerely yours,

A handwritten signature in dark ink, appearing to read "S. H. Wilson".

Samuel H. Wilson, M.D.
Professor and Director

SHW/jr

Enclosures

**Responses to Questions
Submitted for the Record
by the
Subcommittee on Oceanography,
Gulf of Mexico and the
Outer Continental Shelf**

**HEARING: Marine Biotechnology
Investment Act of 1993
April 29, 1993**

**SAMUEL H. WILSON, M.D.
Professor and Director
Sealy Center for Molecular Science
The University of Texas Medical Branch
200 University Boulevard - H51
1023 Sealy-Smith Professional Building
Galveston, Texas 77555-0851**

QUESTION 1: There has been an enormous federal investment in the biotechnology field, with many remarkable advancements. To what extent are the advances in non-marine areas applicable to marine biotechnology? Are techniques readily transferred?

ANSWER 1: Marine biotechnology shares many of the same methodologies and research techniques with other areas of biotechnology. Consequently, marine biotechnology is poised to benefit from advances elsewhere in biotechnology, and vice versa, assuming that the funding increases envisioned in H.R. 1916 materialize. Basic techniques for molecular and genetic research can be transferred readily from terrestrial to marine biotechnology. However, marine biotechnology frequently requires specialized expertise and facilities for handling, culturing, and research on marine organisms.

QUESTION 2: Is increased federal investment needed to maintain U.S. competitiveness in marine biotechnology?

ANSWER 2: There is no question that the U.S. investment in marine biotechnology lags significantly behind that of our international competitors, whether measured by government funding, private-sector expenditures, or a combination of the two. While the U.S. is currently the world leader in marine biotechnology, we cannot expect to maintain our preeminence in the face of determined international competition if our nation fails to respond. We are in serious danger of losing yet another advanced technology -- pioneered here in the U.S. with considerable taxpayer support -- to other nations who have developed concerted national strategies to bring advanced based marine biotechnology to market. The federal government can play a constructive role in enhancing U.S. competitiveness in marine biotechnology through the National Sea Grant College Program, which will improve U.S. competitiveness without resorting to intrusive, government-directed industrial policies.

QUESTION 3: In what areas of research, development, technology transfer, and education is this investment most needed?

ANSWER 3: A balanced program is needed in all these areas: research, development, technology transfer, and education. Each of these areas is interrelated, a comprehensive effort is essential, and a proper balance can be achieved through an independent peer review system as will be established in H.R. 1916.

QUESTION 4: How can partnerships in marine technology among government, industry and academia be best promoted?

ANSWER 4: The National Sea Grant College Program has a proven record of promoting partnerships among government, industry, and academia. Sea Grant is the principal link between the Commerce Department and the academic community, and has developed longstanding relationships with industry through the Marine Advisory Service. Sea Grant has also played a leading role in the development of marine biotechnology, despite a real decline in funding. H.R. 1916 will therefore promote effective partnerships by utilizing the unique capabilities of the Sea Grant Program.

QUESTION 5: What insights can biotechnology provide into ecological and evolutionary problems and how can these lead to better resource management?

ANSWER 5: Marine biotechnology has a host of applications in addressing ecological and evolutionary problems, and in providing new resource management tools. Among these applications in the area of ecology are significant improvements in understanding biogeography and biodiversity, better characterization of the ecological roles of microorganisms, and determination of ecosystem processes relating to environmental change.

QUESTION 6: What are the dangers of biotechnology development for the marine environment? What steps could or should be taken to address these?

ANSWER 6: If proper care is taken, marine biotechnology should pose no significant environmental risk. The greatest concerns have been expressed regarding the release of genetically modified organisms into the marine environment, and these should follow protocols that have already been established for other genetic breeding techniques.

QUESTION 7: What promise does marine biotechnology hold for enhancing the following areas of research and industry: aquaculture; bioremediation; seafood product safety; pharmaceuticals; polymers and lubricants?

ANSWER 7: In my written testimony, I have noted the numerous biomedical applications of marine biotechnology, together with examples from projects that are underway in the Gulf of Mexico region. In aquaculture, marine biotechnology has already been used to increase harvests and improve the health and disease resistance of cultured organisms. In bioremediation, perhaps the most exciting area is the development of microorganisms that are capable of degrading marine pollutants quickly and with less damage to marine ecosystems than chemical or other methods. Marine biotechnology can be applied to seafood safety by developing improved tests for diseases or toxins, and in better understanding the ways in which seafood can be processed more safely. In the pharmaceutical field, marine biotechnology holds the potential to tap into the enormous resource of natural products that exists in the marine environment. New polymers and lubricants are already being developed through marine biotechnology, as demonstrated by the testimony of Mr. Koskan.

STATEMENT OF
NED A. OSTENSO
ASSISTANT ADMINISTRATOR FOR OCEANIC AND ATMOSPHERIC RESEARCH
NATIONAL OCEANIC AND ATMOSPHERIC ADMINISTRATION
U.S. DEPARTMENT OF COMMERCE
BEFORE THE
SUBCOMMITTEE ON OCEANOGRAPHY
MERCHANT MARINE AND FISHERIES COMMITTEE

U.S. HOUSE OF REPRESENTATIVES

APRIL 29, 1993

Mr. Chairman and Members of the Subcommittee:

I am Ned A. Ostenso, Assistant Administrator for Oceanic and Atmospheric Research, National Oceanic and Atmospheric Administration, U.S. Department of Commerce. I appreciate this opportunity to present the Department's views regarding the establishment of a university-based program in marine biotechnology.

Marine biotechnology is the use of marine organisms or their components to provide products (such as polymers, enzymes and other chemicals for use in medicine, agriculture and the chemical industry) and services (such as detoxification of wastes with saline microorganisms, control of biofouling and corrosion, and sensitive measurement with biosensors). It includes aquaculture of food species and encompasses both molecular biology and techniques of traditional biotechnology.

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Marine biotechnology represents a line of activity in the bio-industrial sector that has the potential for broad commercial

development and intense foreign competition. Realizing this potential and meeting international competition will require modern approaches to science and technology, greater dependence on interdisciplinary research, and more intense collaboration and exchange between academe and industry. The National Sea Grant College Program (Sea Grant) is an ideal vehicle for exploiting creativity in academic science for development of marine biotechnology because it fosters programmatic and interdisciplinary approaches to problems and opportunities, promotes interaction and collaboration between universities and industry, and conducts technology transfer. Sea Grant provides primary leadership in marine biotechnology.

The enormity of the oceans gave rise to the traditional view that their resources were almost limitless, that hunting and gathering represented the best approaches for use of these resources, and that proper management would be the primary key to maximum benefit. Recent developments show that in addition to commercial and recreational harvesting coupled with good management, there are other ways through aquaculture and marine biotechnology to use wisely marine species for production of food and other goods, services and processes. I will mention some of these opportunities and provide examples of progress in research and development. I will also touch on foreign efforts.

Even in its infancy, marine biotechnology has yielded significant developments and scientific advancements in a range of scientific disciplines. This progress looks especially promising because of the tremendous importance to the national economy and human well-being of traditional biotechnology based upon use of terrestrial organisms. For example, in the United States annual biotechnical production of antibiotics through use of soil bacteria in bioreactors is an \$8 billion industry. The majority of plant and animal groups are primarily or exclusively marine. Marine organisms are vast in number but have been given only limited attention as targets for technological development.

Scientists at the University of California and other institutions are finding marine organisms to be rich sources of novel chemicals of pharmacological significance. For example, manoalide (isolated from a Pacific sponge) and the pseudopterosins (powerful analgesics from a sea feather coral) represent new chemical and pharmacological classes of substances. Analogues of manoalide, which are not expected to have the side effects of steroids, are in clinical trials as anti-inflammatory drugs. An effective new anti-inflammatory drug could have a worldwide market in the tens or hundreds of millions of dollars annually. Sea Grant advancements in research on natural products is a primary basis for establishment of the new company, OsteoArthritis Sciences, Inc., in Cambridge, Massachusetts, as

well as for letters supporting Sea Grant efforts in marine biotechnology from firms such as Allergan, SmithKline Beecham, Sphinx Pharmaceuticals, Wyeth-Ayerst, Bristol-Myers Squibb and Monsanto.

Researchers studying a class of natural products called oxylipins at Oregon State University showed that marine algae of the Pacific Northwest produce a wide variety of compounds in this class including some mammalian pro-hormones. Their important findings open a number of possibilities for medical research, drug development and commercial production. They have expanded their program to include biochemical engineering for production of oxylipins in bioreactors with algal cells or tissues.

Academic interest in the kinds of exotic secondary metabolites represented by the oxylipins and pseudopterosins extends beyond their application in medicine. What is their role in nature? What insight can they provide to such issues as ecological relationships, biosynthesis, enzymology, chemical communication and symbiosis?

Results from quite different lines of research in marine biotechnology also are being applied in the commercial sector. For example, estuarine bacteria have been adapted to efficiently metabolize, and thereby detoxify, certain organic substances in industrial effluents. Marine microbiologists at Louisiana State

University immobilized the bacteria on a substrate within a chamber (bioreactor) through which a waste stream passes. Results from a test plant treating phenolic wastes showed a 99 percent drop in the concentration of chlorinated phenols. Industry is now using the technology with other types of organic effluents. The university researchers have devised methods to adapt their technology for detoxifying solid waste sites.

Fundamental studies in the South Carolina and Mississippi/Alabama Sea Grant Programs on mechanisms of calcification in mollusk shells have provided practical information in polymer science that is stimulating commercial development. The academic scientists showed that certain components of the proteinaceous matrix of oyster shells inhibit the precipitation of calcium carbonate. Calcium carbonate is a primary component of scale that forms in industrial condensers, boilers and other industrial equipment. Products to control its formation are marketed in enormous quantities. The Sea Grant scientists developed effective analogues of the natural products and processes for synthesizing them. Some of their new materials exhibited the ability to absorb large quantities of water -- a property applicable in a wide range of commercial products such as diapers. However, the most important property of these new materials is biodegradability. Donlar Corporation has been established in Illinois to develop this new line of polymeric materials. It is working with a few of several Fortune 500

companies eager to enter this line of development. (On April 18, 1993 Cable News Network's [CNN] Science and Technology Program focused one of its segments on the academic science behind these advancements.)

Molecular biology and DNA technology have the potential to enhance significantly the use of living marine resources. Obviously, fast-growing, disease-resistant aquacultural strains would be one important application of this technology, but there are others. For example, the diagnosis and control of viral and bacterial fish diseases such as infectious pancreatic necrosis (IPN), infectious hematopoietic necrosis (IHN) and vibriosis are economically important in aquaculture. Several years ago researchers at Oregon State University produced useful vaccines to vibriosis through conventional inactivation of the causative bacterium with heat. Genetic engineering now promises to provide more specific and effective vaccines. The gene for the outer membrane protein of one pathogen in the genus *Vibrio* has been cloned into another easily-grown bacterium. This is making possible the production of highly effective vaccines because this membrane protein is immunogenic. Similar advancements have been made with the IHN virus.

Many approved methods used for the detection of bacteria and determination of water quality and safety of raw seafood are slow, non-specific and labor intensive. To help alleviate this

problem, researchers are developing rapid assays for certain pathogenic bacteria. The assays are based on techniques in molecular biology such as DNA probing. Because each species of living organism has certain unique sequences of DNA, and these sequences tend to pair or form bonds with complementary sequences of DNA, highly specific reagents (DNA probes) can be produced for quickly identifying and quantifying organisms in a test sample. Many marine applications of this technology are possible. For example, rapid unequivocal assays for human pathogens in seafood and fishing waters could improve seafood safety and provide the basis for delineating safe fishing waters more precisely and less conservatively.

I have given you a few examples of modern biotechnical methods of using marine resources and advancing marine science and industry. Developments of this kind in the United States, which have resulted from a low level of federal investment, have not gone unnoticed abroad -- particularly in Japan. For example, a few years ago Unitika bought non-exclusive rights to and developed patented technology resulting from research on marine materials at the University of Delaware. As a result, it is marketing a wound-healing bandage for burn victims that is made from chitosan, a natural polymer derived from crustacean shells.

Japan is taking an aggressive role in marine biotechnology through its Ministry of International Trade and Industry. In

collaboration with major industrial firms, Japan will invest in excess of \$200 million over a decade in the Marine Biotechnology Institute (MBI). The objective of the MBI is to be the first full-scale marine biotechnology research and development base, not only nationally, but globally. It is based on the premise that marine biotechnology is the "greatest remaining technological and industrial frontier." (See, "Prospectus for Establishment of Marine Biotechnology Institute (1987)", Committee for the Marine Biotechnology Institute, Ministry for International Trade and Industry, Tokyo.)

Japanese researchers at the Tokyo University of Agriculture and Technology developed methods that induce marine algae to produce large amounts of the enzyme superoxide dismutase (SOD). SOD is a natural antioxidant that converts oxygen radicals into ordinary oxygen molecules. It can be used in a range of medical, cosmetic and food applications. The potential annual market for SOD in the United States has been estimated at \$700 million. Other Japanese research has demonstrated that marine microorganisms biosynthesize novel anti-malarial antibiotics, anti-tumor polysaccharides and glucan-degrading enzymes which may be useful in industrial or dental applications. As a result, the Japanese researchers have high expectations that studies of marine microorganisms will prove to be as fruitful as those of their terrestrial counterparts in regard to production of medicinal compounds and industrial materials.

Many areas of marine research have the potential to advance science and set the stage for developing new biotechnical products and services for the future and to train students for careers in high technology. None is receiving adequate research attention. Among the topics of opportunity in marine biotechnology are the following:

- natural function of bioactive compounds,
- pharmacological properties of bioactive compounds and their mechanisms of action,
- biochemistry and physical properties of enzymes and other biopolymers,
- DNA technology for genetically engineering marine organisms of all types -- plants, animals and microorganisms,
- cell culture of invertebrates and microorganisms and associated physiology and nutrition,
- biochemical engineering for bioreaction, photo-bioreaction, fermentation and immobilized biocatalyst reaction,
- biosensors, and
- modern quality control and diagnostic reagents for seafood and fishing waters.

All of these topics require or could benefit from interdisciplinary approaches to developing the fundamental science on which new technologies can be based.

In addition to advancements in disease control, modern aquaculture needs fundamental advancements in nutrition, endocrinology, reproductive physiology and pheromonal communication of aquacultural species. A range of scientific and engineering advancements also are needed to establish reliable and economic technology for commercial production in recirculating systems. Such issues should be addressed in a marine biotechnology program.

Sea Grant also has proved itself effective in advancing and developing technology for aquaculture where multi-disciplinary research is essential. For example:

The science and technology has been developed for synchronizing spawning of abalone and controlling settlement of their larvae so that hatcheries could be developed for these mollusks which now are cultured commercially in California.

Science and production technology has been developed for a burgeoning new industry in aquaculture of hybrid striped bass. Annual production is now over 1 million pounds with over 10 producers in the mid-Atlantic region.

A fast-growing, more attractive hard shell clam has been developed which is the basis of a \$7 million aquacultural development in South Carolina.

A triploid oyster has been developed that makes possible a year-round rather than a seasonal oyster industry and has contributed to the revival and stabilization of the oyster industry on the West Coast.

The science and technology has been developed for controlled farming of seaweeds that produce industrial polymers. The polymer carrageenan from production of these farms is the basis for hundreds of millions of dollars of U.S. products.

Two "all-fish" expression vectors have been developed that will be useful in genetic engineering of fish and which have already made contributions to DNA technology. For example, the B-actin gene of carp was shown to be nearly identical to the B-actin gene of mice. Because of this similarity, fertilized fish eggs costing approximately \$3 each can be used in genetic engineering research instead of transgenic mice embryos that cost from \$300 to \$3000 each.

Molecular technology has been developed for delineating fishery stocks and populations.

Sea Grant's research in support of marine biotechnology is directly relevant to major goals of the Department of Commerce:

- to increase U.S. exports of goods and services,
- to promote the development and application of science and technology in U.S. industries, and
- to promote the development and growth of oceanic and atmospheric industries.

NOAA supports expanding marine biotechnology research. However, any legislation which would establish a large panel for competitive review of proposals may result in an unwieldy and inefficient administration of the program. Instead, the National Sea Grant Office should be required to use study panels of appropriate size and make-up by methods similar to those of the National Science Foundation or the National Cancer Institute.

In closing, it should be noted that marine biotechnology is a topic of special emphasis in "Biotechnology for the 21st Century," a 1992 report of the Federal Coordinating Council on Science, Engineering and Technology. With this hearing it is now apparent that the Legislative and Executive branches are in synchrony in considering this important area of science and technology.

Thank you Mr. Chairman and Members of the Subcommittee for this opportunity to express the views of the Department. I would be pleased to answer any questions you may have.



UNITED STATES DEPARTMENT OF COMMERCE
National Oceanic and Atmospheric Administration
Silver Spring, MD 20910

OFFICE OF OCEANIC AND ATMOSPHERIC RESEARCH

JUL 23 1993

The Honorable Solomon P. Ortiz
Chairman, Subcommittee on Oceanography,
Gulf of Mexico, and the Outer Continental Shelf
Committee on Merchant Marine and Fisheries
House of Representatives
Washington, D. C. 20515-6230

Dear Mr. Chairman:

Thank you for your letter regarding marine biotechnology. The four-page enclosure provides my responses to the Subcommittee's questions. I appreciate the opportunity to respond to the inquiries about opportunities in marine biotechnology and how the legislation under consideration would affect the National Sea Grant College Program. I stand ready to provide additional information if needed.

Sincerely,

Ned A. Ostenso
for Ned A. Ostenso
Assistant Administrator

Enclosure



Ned A. Ostenso's Answers to Questions (April 29, 1993) of the Subcommittee on Oceanography, Gulf of Mexico, and the Outer Continental Shelf

Question: How would a program of the size proposed in the Marine Biotechnology Program Act impact the Sea Grant program? Would this detract from other Sea Grant research areas?

Answer: A program of the size proposed would generate a range of new approaches to using marine resources and would be a positive influence on academic science, the National Sea Grant College Program, and NOAA. It would not detract from other Sea Grant research areas because almost all of them, especially fisheries research and environmental studies, are conducted in a context broader than Sea Grant and are complementary to other major programs within NOAA and in other federal agencies.

Question: We have heard a lot about the Japanese investment in marine biotechnology and your testimony expanded on some of the advancements they have made. Is there sufficient interaction and information transfer between the United States and Japan? What mechanisms are in place to ensure this interaction?

Answer: There is sufficient interaction between the United States and Japan on aquaculture (and undersea technology) through the United States-Japan Cooperative Program in Natural Resources (UJNR). The United States has benefitted from this interaction more than Japan. There is insufficient interaction and exchange of information on marine biotechnology outside of aquaculture. I will recommend instituting a UJNR panel on marine biotechnology to ensure proper interaction with Japan.

Question: I appreciate your support of Sea Grant's role in federal marine biotechnology research, but I am concerned that NOAA has requested no funds to enhance the Sea Grant involvement, even though increases were requested for two other Presidential initiatives. Instead, it has been left for Congress to take the initiative. Can you explain why NOAA chose not to pursue this opportunity on its own?

Answer: NOAA put forward a budget initiative in biotechnology for fiscal year 1994, but the Office of Management and Budget was unable to include it in the President's budget. (For the first time since 1981 OMB was including a request to fund Sea Grant's marine advisory program. This required adding \$17 million for fiscal year 1994 to OMB's previous request for Sea Grant just to reflect level funding as set by Congress in fiscal year 1993.) As a result of the Federal Coordinating Council on Science, Engineering, and Technology's recent study on biotechnology for the future and the including of marine biotechnology as

a special focus, NOAA and the President are discussing NOAA's role in support of marine biotechnology.

Question: Is increased federal investment needed to maintain U.S. competitiveness in marine biotechnology?

Answer: A report in draft at the University of Maryland's Center for Public Issues in Biotechnology states that "unless there is a major effort to more greatly focus U.S. activity in this area, advances in the United States will be limited to the occasional chance discovery of a process, activity or application." The same report estimates that the Japanese Government invests \$180 million annually in marine biotechnology. The United States is at a disadvantage in aquacultural research and production. Greater investment in this field would take advantage of existing infrastructure to provide technology that could set U.S. competition in aquaculture on the upswing.

Question: In what areas of research, development, technology transfer, and education is this investment most needed?

Answer: This investment in biotechnology, including aquaculture, is most needed for research, education, and technology transfer in (1) molecular genetics to provide technology for modifying and enhancing the growth and biosynthetic characteristics of marine plants, animals, and microorganisms, (2) biochemical engineering for developing fermentation, bioreactor, and bioprocessing technology with marine organisms or their components, (3) bio-organic chemistry and pharmacology for identifying and defining properties, mechanisms of action, and biosynthetic pathways of novel marine compounds important in medical research and as models for new drugs, (4) chemical, physical, and production studies of biopolymers and enzymes as models for new industrial materials, (5) molecular technology for identifying, in aqueous and biological samples, marine microbial pathogens of humans and aquacultural species and for controlling their spread, (6) reproductive physiology and endocrinology of aquacultural species for controlling and synchronizing reproductive and developmental processes, (7) engineering of closed aquacultural systems for maintaining water quality and managing effluents and wastes, and (8) halophyte biology and culture to provide plants and technology for restoring degraded coastal environments and for producing food and forage in saline soils.

Question: How can partnerships in marine biotechnology among government, industry and academia be best promoted?

Answer: The Sea Grant College Program Act promotes partnerships by requiring at least one third of the cost of Sea Grant programs to be paid for with non-federal matching funds. These funds come from state and local government, industry, and academic institutions. The National Sea Grant Office further promotes partnerships by encouraging state and regional Sea Grant programs to establish relationships with the projected users in advance of starting research. Regional and national Sea Grant managers promote interactions by bringing representatives of government, industry, and academia together in workshops to consider problems and opportunities and plan for the future. International conferences such as the International Marine Biotechnology Conference, which has been held twice, (once in Tokyo, once in Baltimore and next year in Norway) promote interaction among professional sectors. Additional mechanisms for promoting interaction need to be considered.

Question: What insights can biotechnology provide into ecological and evolutionary problems and how can these lead to better resource management?

Answer: Techniques of molecular biology can be used to indicate the genetic similarities of organisms. Therefore, scientists could separate anadromous fishery stocks by area of origin. This potentially would allow management of fishing with more precision than now possible. Application of these techniques also would enhance assessing the contribution of juveniles from stocking programs to wild fisheries. And, they could be used to track larval fish in nature and help define processes controlling recruitment.

Question: What are the dangers of biotechnology development for the marine environment? What steps could or should be taken to address these?

Answer: There is some chance that strains with altered or added genes could compete reproductively with natural strains and reduce genetic diversity in the wild. Such potentialities can be avoided by restricting the introduction of altered organisms into the environment and regulating their confinement in experimental or production facilities. Such issues are being considered as part of the review of intentional introductions as required by the Nonindigenous Aquatic Nuisance Prevention and Control Act of 1990. This review includes, specifically, the concern about escapement from aquaculture facilities.

Question: What promise does marine biotechnology hold for enhancing the following areas of research and industry: aquaculture; bioremediation; seafood product safety; pharmaceuticals; polymers and lubricants?

Answer: Biotechnology holds the promise of further enhancing aquaculture through production of cloned vaccines for animal diseases, development of disease-resistant strains with improved growth and food conversion characteristics, control of reproductive processes at a fundamental level, design and demonstration of recirculating containment systems, and advancement of a range of science and technology needed to culture marine finfish. The marine aquacultural industry has the potential to employ tens of thousands of additional workers and reduce imbalance in trade of seafood by hundreds of millions of dollars.

Use of marine species in bioremediation is just beginning to develop, but already there are applications using them to detoxify organic pollutants such as petroleum and toxicants in industrial brines. Current efforts focus primarily on the isolation and culture of microorganisms capable of carrying out specific chemical transformations. The metabolic pathways that lead to these transformations can then be identified, the genetic basis determined, and the organisms cultured or genetically enhanced and used in bioreactors to detoxify pollutants.

Marine biotechnology has the potential of providing rapid assays for viral, bacterial, and chemical contaminants in seafood and thereby making implementation of Hazard Analysis and Critical Control Point (HACCP) procedures in the seafood industry economic and reliable. For example, Sea Grant research developed a rapid enzyme-linked immunosorbent assay (ELISA) for the detection of *Vibrio cholerae*, the bacterium that causes cholera. A commercial firm has adapted this technology to produce a small hand-held kit into which a dipstick, previously exposed to sample, can be inserted. A squeeze of the fingers exposes the sample to diagnostic reagents. Within ten minutes a positive sample produces a color reaction discernable to the naked eye. The company has sent millions of these kits to South America where they are being used to combat an epidemic of cholera.

Marine biotechnology holds promise for advancing science and providing the technical basis for products, processes, and job creation in the pharmaceutical and chemical industries. For example, the natural products and biodegradable polymers you heard about from the presidents of OsteoArthritis Sciences, Inc. and Donlar Corporation respectively at the April 29 hearing on marine biotechnology have the potential to provide hundreds of millions of dollars annually of U.S. products to international markets and to employ hundreds of people.

**Marine Biotechnology:
A National Potential in Need of National Attention**

Oskar R. Zaborsky, Ph.D.
President
OZCOM International Inc.
P.O. Box 7604
McLean, VA, 22106

Comments for the
Committee on Merchant Marine and Fisheries
Subcommittee on Oceanography, Gulf of Mexico and the Outer Continental Shelf
April 29, 1993

The United States is the undisputed global leader in biotechnology (both in science and commerce) because several agencies in the federal government had the foresight to establish programs to support relevant R&D. In particular, the National Science Foundation (NSF) and the National Institutes of Health (NIH) deserve much credit. NSF also supported generic applied research in the mid 1970s that catalyzed further commercial developments in biotechnology on agriculture, specialty chemicals and materials, and bioprocess engineering. NIH, on the other hand, supported R&D that led to many advances in the diagnostic and pharmaceutical industries. Some things clearly worked and the timing was right.

Now it is time for federal agencies to support biotechnology of relevance to other industries including those dealing with marine resources. Other countries, notably Japan, have launched a number of bold initiatives. Japan's crown jewel of marine biotechnology is the Marine Biotechnology Institute Co., Ltd (MBI) that was established in 1988 by the Ministry of International Trade and Industry (MITI) and 24 major companies. An even more ambitious effort initiated by MITI is the Research Institute of Innovative Technology for the Earth (RITE), an organization similar to MBI but totally dedicated to environmental problems and new business opportunities for Japan. RITE includes marine biotechnology projects such as biological CO₂ fixation and hydrogen production.

Barriers for U.S. Marine Biotechnology

Several barriers prevent the U.S. from realizing the full potential of marine biotechnology for commercial purposes (Table 1).

Table 1. Barriers for Marine Biotechnology

- Inadequate Funding
- Inadequate Knowledge Base
 - Unorganized information base
 - Limited generic applied research - bioprocess engineering
- Personnel Limitations
- Regulatory Uncertainties - Environmental Release of Transgenic Animals
- Unsettled Patent Issues
- Public Rejection of Biotech Products

Inadequate Funding

As in other areas of biotechnology, the federal government is the primary force behind research in marine biotechnology. However, funding for this area is minuscule. Total federal funding for marine biotechnology for Fiscal Year (FY) 1992 was only \$43.9 million. Funding for FY 1993 increased by about \$6 million. As reference, total federal funding for biotechnology in 1992 was \$3,759 million. Thus, the percentage devoted to marine biotech in 1992 was only 1.2%; for 1993, it remains the same. While most can appreciate the tight fiscal situation, without greater investment it is doubtful that the U.S. will be able to maintain its present position or even come to parity with Japan's more applied and dedicated efforts. An investment of only 1% is clearly below that made by U.S. industries (e.g., pharmaceutical, diagnostic, and computer) that are competitive internationally (normally investing 5-10% of their sales in R&D). Clearly a 3-5 fold increase in total federal funding for marine biotechnology is not unreasonable given its potential. At any level, priority should be given to programs that foster technology development and commercialization such as the Department of Commerce's Sea Grant Program.

Inadequate Knowledge Base

While we know many things about the marine environment and its varied life forms, unfortunately we do not know how to use that knowledge in a dedicated fashion for producing new goods. Foremost, and costing little, is the need to gather, organize, and disseminate key

information on marine biotechnology -- especially information that is commercially relevant. Such an effort could be undertaken with minimal funding yet be of immense value to industry, government, and academia. The need for organizing information has been recognized in other areas of biotechnology, most notably the human genome program. A non-profit information center or clearinghouse should be established.

There is also a need for generic applied research and engineering centers, including a facility dedicated to marine bioprocess engineering. This is especially critical since many interesting bioactive compounds found to date are difficult, if not impossible, to synthesize chemically. Additionally, these bioactive compounds are also difficult to isolate from natural sources (algae, sponges, etc.) because of logistic complexities (i.e., having to collect living organisms from difficult-to-reach places) or limitations in productivity. What is needed is a marine bioprocess engineering center that will be able to produce sufficient amounts of "interesting" compounds for further exploration by industry through mass culturing of the particular organisms or from cells that contain the bioactive compounds of interest. If sufficient amounts of these bioactive compounds were available, derivatives -- at times even more effective than the natural substance -- could be made.

Personnel Limitations

Only a small group of marine biotechnologists now exists in the U.S. and a new cadre of people is needed with knowledge of both the new sciences, especially molecular biology, and the traditional marine sciences. While it is important to have capability in basic research, it is critical to have well-trained people in the U.S. who can translate the exciting research findings into technologies and products. New training programs -- with a heavy involvement by industry -- need to be established.

Regulatory Uncertainties

The frenzied days of recombinant DNA are behind us, but there are still numerous regulatory uncertainties. Many aspects of field testing transgenic animals have not been resolved, and the release of any new life form into the marine environment will be controversial. The commercialization of transgenic fish is a global uncertainty. Federal regulatory agencies need to address these issues with an active involvement by industry and public interest groups.

Unsettled Patent Issues

Major differences in patent policies exist from country to country, especially regarding the patentability of transgenic animals. One can only hope that the patent system will be much

more defined, uniform, and time-responsive when marine biotechnology will be in full bloom. Congress, through OTA, is again examining biotechnology patent issues as a result of developments in the human genome project.

Public Rejection of Biotech Products

Whether we in science like it or not, there is a growing sentiment not to accept certain products even if they are efficacious and superior to natural counterparts. Clearly, biotechnology products in the health care arena have not been rejected by the public because there is a clear distinction of performance and benefit. However, the situation is different for agricultural biotechnology products. Bovine somatotropin, a product acceptable to the FDA, has not been greeted with enthusiasm by some. More recently, the highly charged question of long-term human safety associated with transgenic plants as foods has come to the surface. The question of public acceptance of transgenic fish has yet to be raised. Clear dialogue among the various groups in government, industry, and the public is needed.

Capturing the Fruits of Research

Marine biotechnology represents one of the greatest frontiers of intellectual and commercial activity for the remaining years of this century and for decades to come in the 21st century. The positives clearly outweigh the negatives. If we are to reap the benefits, however, the federal government, through its various agencies, needs to support strongly this emerging technology and the underlying sciences. Increased knowledge and the wise use of marine resources will also safeguard the fragile nature of the marine environment and its biological diversity for future generations.

* * * * *

Dr. Zaborsky is the President of OZCOM International Inc., an information services and management consulting firm dealing with the life sciences industries. He is the former Director of the Board on Biology, National Research Council - National Academy of Sciences, Washington, D.C.

His efforts in marine biotechnology include: member of the National Academy of Sciences Committee on Biotechnology Applied to Naval Needs (*Marine Biotechnology: Basic Research Relevant to Biomaterials and Biosensors*, 1985); principal investigator for NSF's Division of International Programs assessment of Japanese marine biotechnology (*Marine Biotechnology in Japan*, 1989); participant at Biotechnology Policy Forum on marine biotechnology (1991); and co-editor of a new series, *Advances in Marine Biotechnology*, the first volume of which is devoted to bioactive pharmaceutical compounds (1993).



